Twenty-fourth Annual Meeting
San Francisco, June 18-22, 1958

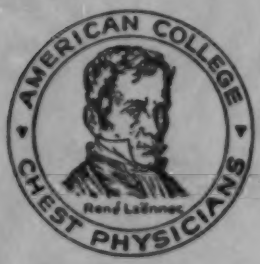
VOLUME XXXIII NUMBER 3

DISEASES

of the

CHEST

OFFICIAL PUBLICATION



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Fifth International Congress on Diseases of the Chest
Tokyo, Japan — September 7-11, 1958

DISEASES *of the* CHEST

OFFICIAL PUBLICATION
OF THE
AMERICAN COLLEGE OF CHEST PHYSICIANS

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(1) Feinberg, A. R., and Feinberg, S. M.: J.A.M.A. *160*:264, 1956. (2) Schwartz, E.: J. Allergy *26*:206, 1955. (3) Skaggs, J. T.; Bernstein, J., and Cooke, R. A.: J. Allergy *26*:201, 1955. (4) Barach, A. L.; Bickerman, H. A., and Beck, G. J.: Dis. Chest *27*:515, 1955.

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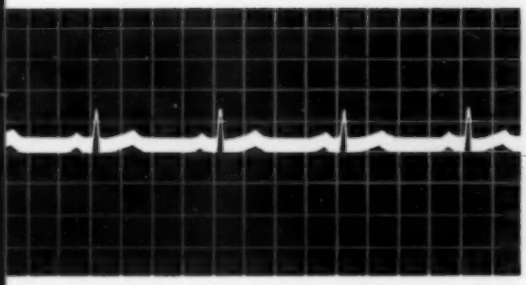

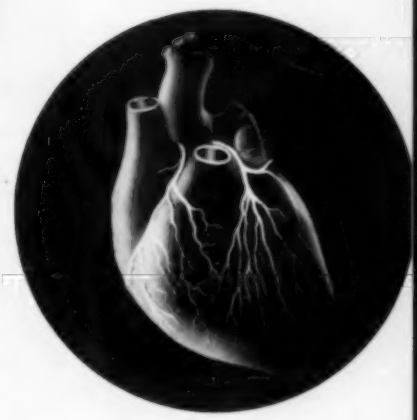

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1. Aravanis, C., and Luisada, A. A.: Am. J. Cardiology, in press.

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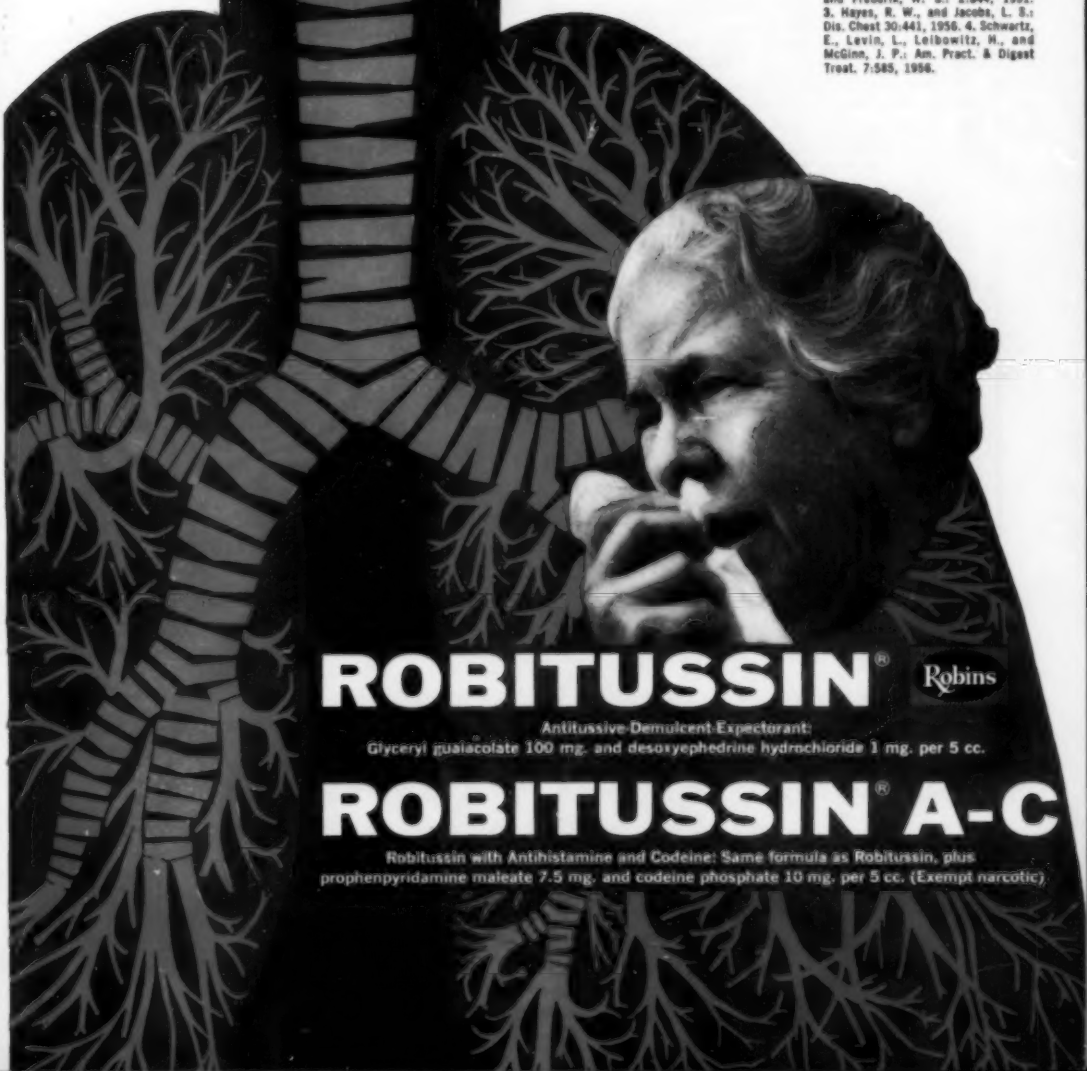
References:

1. Blanchard, K., and Ford, R. A.: Clin. Med. 3:961, 1956. 2. Cass, L. J., and Frederik, W. S.: 2:844, 1951. 3. Hayes, R. W., and Jacobs, L. S.: Dis. Chest 30:441, 1956. 4. Schwartz, E., Levin, L., Leibowitz, H., and McGinn, J. P.: Am. Pract. & Digest Treat. 7:585, 1956.



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LB-2 Monitor

LB-1 Analyzer

5-49

WHEN YOU TREAT INFECTIONS IN PATIENTS SUCH AS THESE

- debilitated
- elderly
- diabetics
- infants, especially prematures
- those on corticoids
- those who developed moniliasis on previous broad-spectrum therapy
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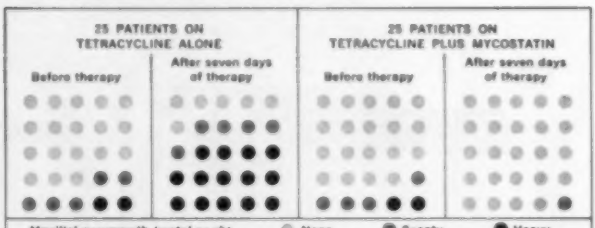

Childs, A. J.: British M. J. 1:660 1956.

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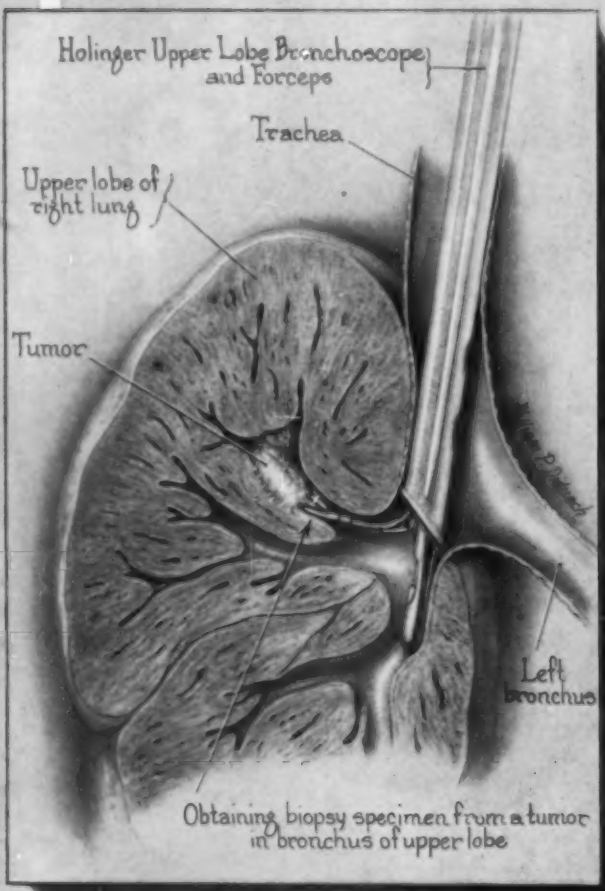

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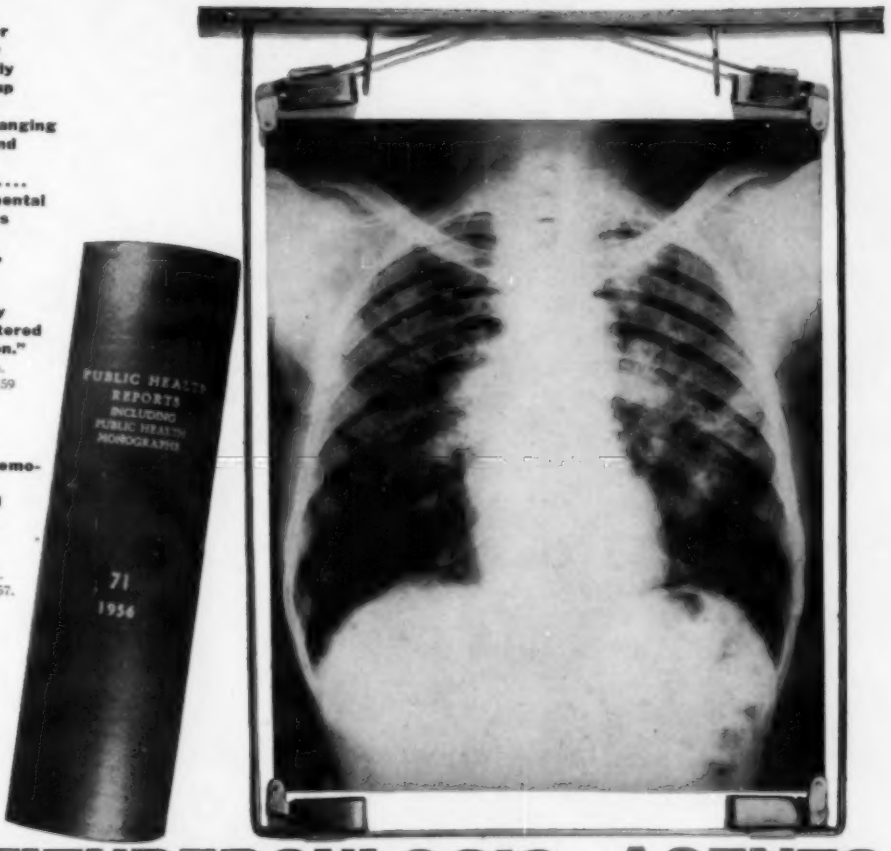
Peck, W. M.: Pub. Health Rep. 71:1159 (Dec.) 1956.

"Prolonged combined chemotherapy [is] the accepted method of treatment."
Chapman, P. T.: J. Kentucky M. A. 55:235 (March) 1957.



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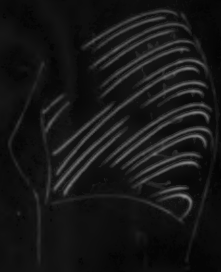
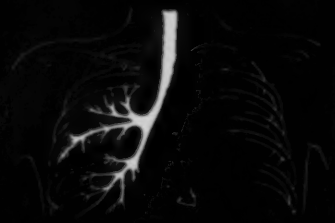


Using Camera A or B

Silicosis research and bronchography



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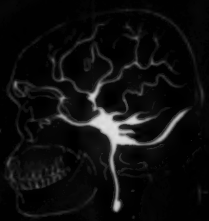
Cerebral angiography



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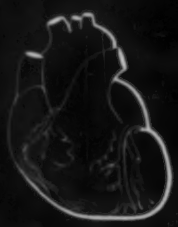
Angiocardiography, angiography



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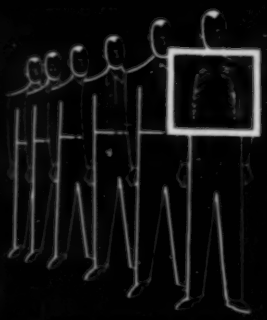

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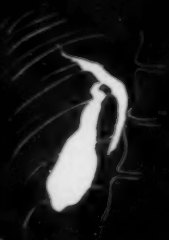
G. I., kidneys and gall-bladder radiography



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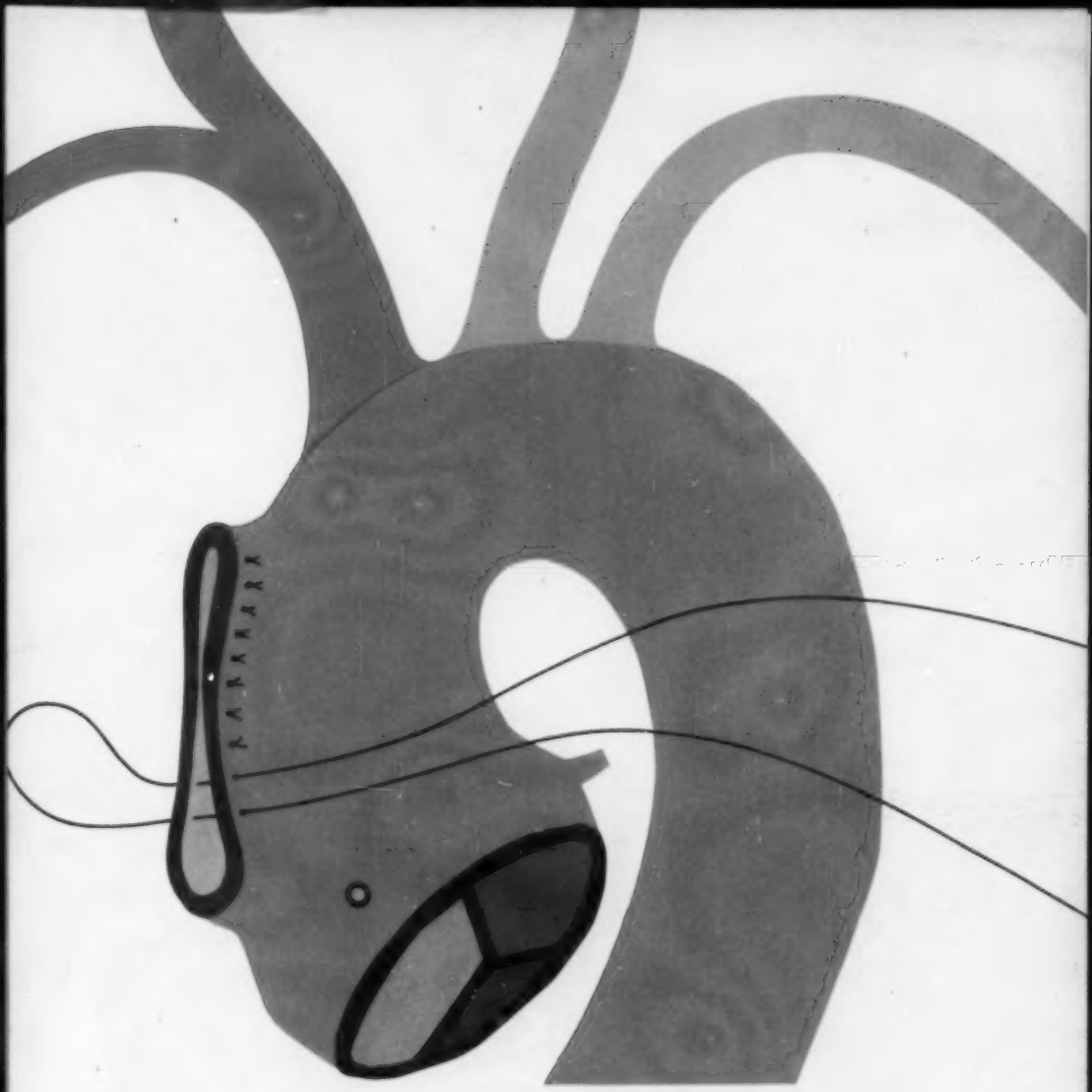

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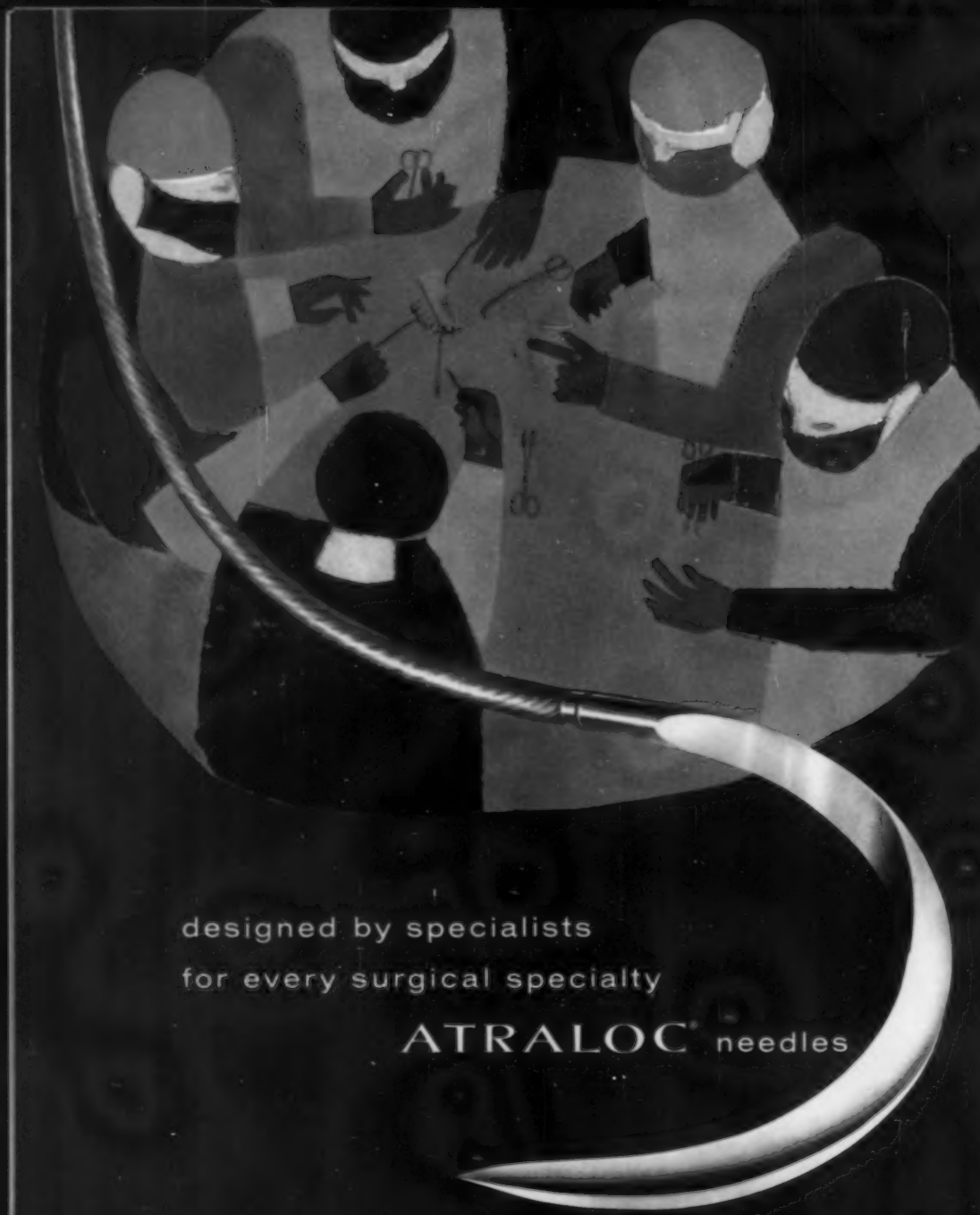

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Potassium para-aminosalicylate (KPAS) was administered to 120 patients with tuberculosis.

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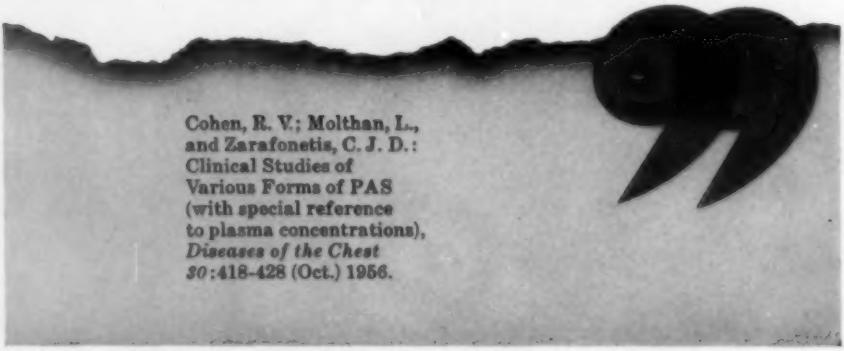
Plasma PAS concentration studies revealed that KPAS is more rapidly absorbed and yields significantly higher values than either PAS or NaPAS.

KPAS is ideally suited for use in patients with congestive heart failure, pregnancy, or other situations in which use of the sodium salt is precluded.

The 10 per cent solution of KPAS was used for "desensitizations" of those who had acquired sensitivity reactions to PAS compounds.

It is concluded that KPAS is superior to other forms of PAS.



Cohen, R. V.; Molthan, L., and Zarafonetis, C. J. D.: Clinical Studies of Various Forms of PAS (with special reference to plasma concentrations), *Diseases of the Chest* *30*:418-428 (Oct.) 1956.

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a rapidly eliminated bronchographic medium...

less irritating—rarely penetrates the alveoli

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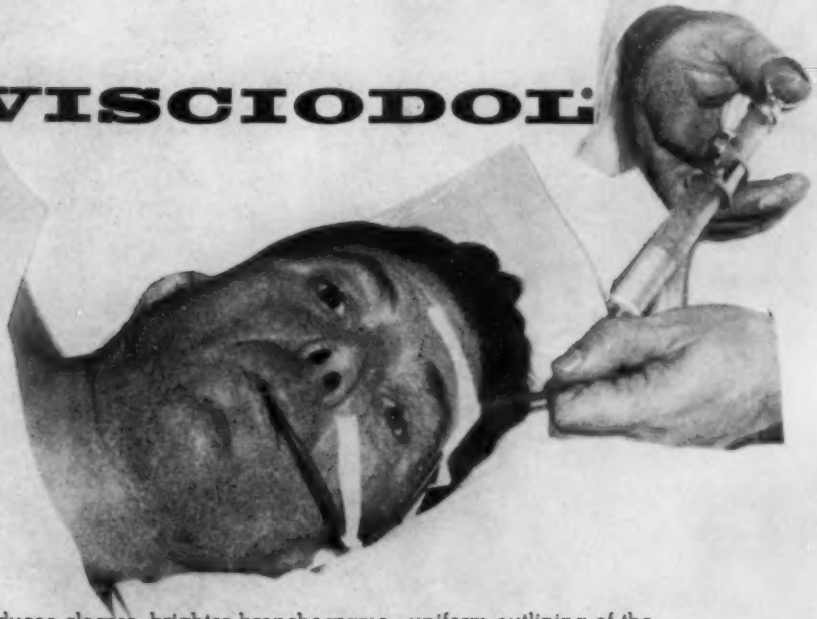

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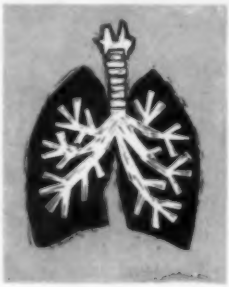
ASTHMA

and allergic disorders



HERE ARE THE RESULTS WITH ORAL KENACORT:[1-5]

Number of patients	Daily maintenance dosage range (mg.)	Results		
		Excellent or good	Fair	Poor
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Perennial rhinitis 4	2-6	4		
Infective asthma 3	4-16	3		
Allergic asthma 2	2-10	2		
Drug allergy 1	2-16	1		

KENACORT IS A NEW, IMPROVED CORTICOSTEROID WHICH PRODUCES EXCELLENT CLINICAL RESPONSE

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- *without unnatural psychic stimulation*
- *and on a lower daily dosage range*

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1. Reports to the Squibb Institute of Medical Research, 1957. 2. Sherwood, H., and Cooke, R. A.: J. Allergy 28:97, 1957. 3. Hellman, L., et al.: American Rheumatism Association. Interim session, Nov. 23, 1956. 4. Berntsen, C. A., Jr., et al.: New York Rheumatism Association. Annual meeting, April 9, 1957, New York. 5. Freyberg, R. H., et al.: International Congress on Rheumatic Diseases, June, 1957, Toronto.

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ALEVAIRE® aerosol in the home

in bronchiectasis–

*"Thick, yellow, solid sputum which had been expectorated with difficulty became thin, colorless and liquid sputum which was expectorated with ease and gradually diminished in volume. Labored breathing and insomnia, . . . soon were replaced by easy respiration and ability to enjoy normal restful sleep."**

CASE REPORT

A typical Alevaire case history–C. S., 31 year old male with bronchiectasis and sinusitis, had had pneumonia six times. He had a continuous thick purulent postnasal drip and thick, yellowish green sputum; he expectorated at least a cupful of sputum each morning on arising. The patient was weak and debilitated, with chills and low grade fever. Bronchograms revealed advanced bronchiectasis. Antibiotics, postural drainage and expectorant cough mixtures had not helped.

Alevaire therapy was begun with one hour of direct nasal inhalation every day. After the first treatment the patient expectorated a large amount of sputum and definitely breathed easier. The nasal passages began to open, and with subsequent treatments both the sinusitis and the bronchiectasis improved. He began to breathe easier through the nose and to expel bronchial secretions more readily. His appetite improved and he felt stronger.

At the end of fourteen days he was almost completely symptom free. Alevaire was continued each night for short periods at bedtime, and the patient remained completely free of symptoms except for a light morning expectoration.

*Miller, J.B., et al.: Ann. Allergy, 12:611, Sept.-Oct., 1954.

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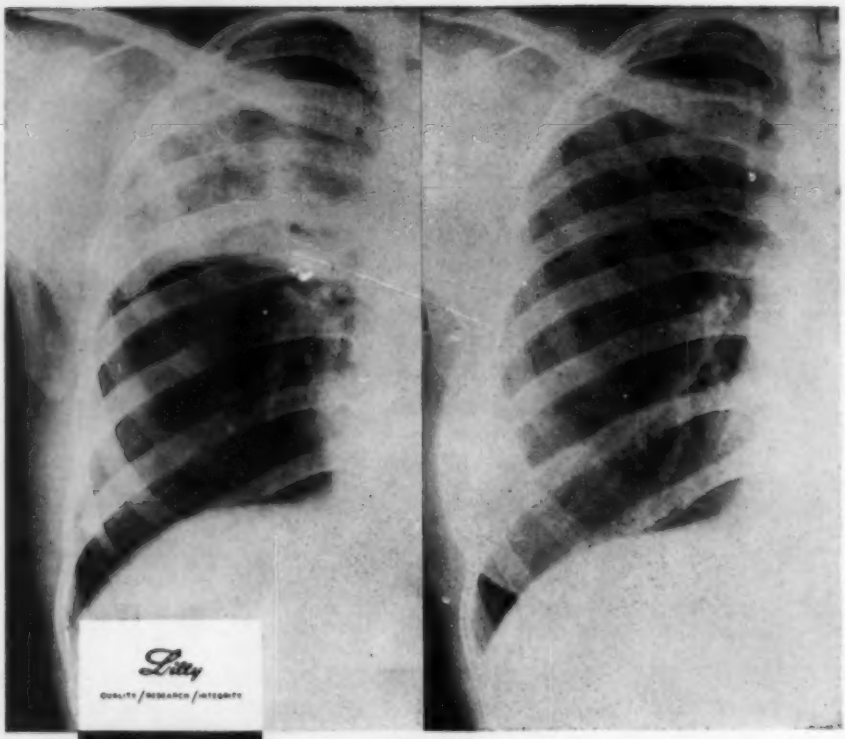

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for tuberculosis

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DISEASES of the CHEST

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Recent Advances in Bronchography*

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Recent advances in bronchography have occurred as a result of new bronchographic media and technique. These advances have improved the quality of bronchography to such an extent that small bronchial lesions are more readily seen. A method of correlating these bronchographic defects with their histological appearance has increased our knowledge of the significance of these defects. The first part of this paper will discuss the recent advances in bronchographic media and technique and the second portion will describe the finer bronchographic defects and their histological appearance.

PART I

Bronchographic Media and Technique

There are two schools of thought in regard to the type of bronchogram which is considered the most valuable from a diagnostic viewpoint. The first school maintains that a good bronchogram should demonstrate patency between the trachea and the alveoli of each segment; that is, they seek alveolar filling to demonstrate this patency. Those belonging to the second group prefer to have the bronchial tree well outlined with a uniform coating from the trachea to the bronchioles without alveolar filling. Residues remaining in the lung after bronchography, whether opaque or non-opaque, can produce foreign body reactions. Foreign body reaction has been demonstrated due to the non-opaque peanut oil in Dionosil Oily,[1]† to carboxymethyl cellulose in Dionosil Aqueous[2]† and to the residual oil following instillations of Iodochlorol,[3]‡ as well as Lipiodol.[4]§ This reaction is much greater in areas where there are larger amounts of alveolar filling.[2] To avoid foreign body reaction in the lungs of patients, a technique of bronchography and a type of bronchographic medium must be used which do not produce alveolar filling. Alveolar filling is not essential for a thorough examination of the bronchial tree by bronchography.

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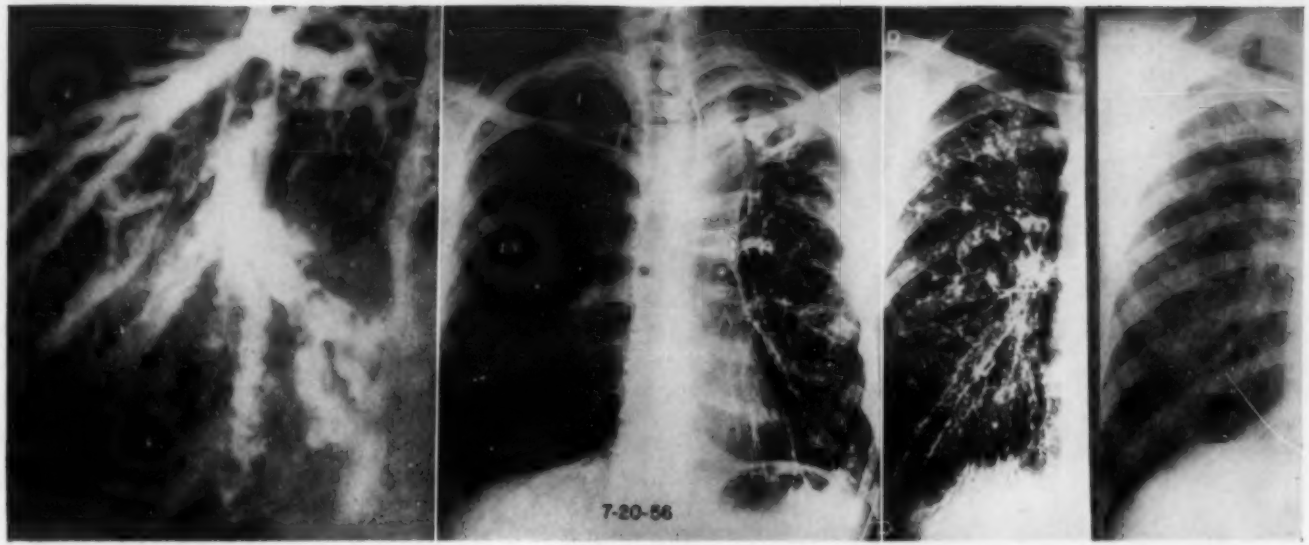

FIGURE 1 FIGURE 2 FIGURE 3A FIGURE 3B

Figure 1: Filling Beyond Areas of Obstruction. A benign tumor in the common basal stem bronchus produced sufficient obstruction to cause intermittent basilar pneumonitis and acute recurring bronchitis.—*Figure 2: Metras Catheter Used in Routine Bronchography.* To facilitate filling of apical cavities or spaces, the Metras catheter is used to fill the space before the catheter is withdrawn to allow completion of the unilateral bronchogram. This patient has a persistent apical space following a previous pulmonary resection for pulmonary tuberculosis.—*Figure 3: Residual Oil Remaining in the Lungs After Dionosil Oily Bronchogram.* Plain peanut oil in Dionosil Oily was substituted with iodinated peanut oil (Iodochlorol) for a right bronchogram so that after absorption of propyliodone, the oil remaining in the lungs can be seen on the roentgenogram. (*A*) Notice the residual oil on the roentgenogram taken twelve days later. (*B*) This residue is greater than is usually seen after Visciodol. Presence of oil remaining in the lungs after the use of Dionosil Oily has also been confirmed histologically.[7]

Alterations in the viscosity and surface tension of Lipiodol produced by the addition of sulfanilamide powder, that is Visciodol, permits a continuous and uniform coating of the entire bronchial tree with minimal alveolar filling. These outlines show good contrast in areas of pulmonary disease and usually produce a double contrast effect which permits small bronchial lesions to be readily seen. We have had no great difficulty in peripheral filling of diseased bronchi or filling beyond areas of partial obstruction (Figure 1) unless these bronchi are filled with mucopurulent secretions. Visciodol, being a more viscous medium than the Dionosils or ordinary iodized oils, flows slower through the small bronchi; therefore sufficient time must be allowed for adequate bronchial filling.

Allergic reactions in the form of uticaria by sulfanilamide powder occurred in only two patients after 500 bronchograms and these have responded well to antihistaminic therapy. Other types of postbronchographic reactions were less frequent with Visciodol than with Dionosil Oily. Bronchograms of diagnostic quality with outlining of all segments in each lung were obtained in 78 per cent of examinations with Dionosil Oily as compared to 89 per cent with Visciodol. This increase of approximately 10 per cent in the incidence of bronchograms with greater diagnostic value warrants the continued use of Visciodol. Bronchography at our hospital is used in the preoperative work-up in a large percentage of the patients prior to pulmonary resection. Experience with Visciodol now exceeds 500 examinations with excellent results.

The technique of selective bronchography using the Metras or Thompson catheters[5] to fill specific segmental bronchi is of value in the occasional case where a segment was not outlined on a previous examination. When difficulty in filling a small apical space, cavity or diseased bronchus is anticipated, the selective technique is suggested in which an appropriate Metras or Thompson catheter is used to fill this defect. The catheter is then withdrawn sufficiently to permit completion of the routine unilateral bronchogram (Figure 2) thus obviating the need for a repeated examination. Since this technique may be associated with an increase in alveolar filling, it is essential that a medium be used, such as Visciodol, which has little tendency to flow into the alveoli.

Following bronchography an aerosol using a bronchodilator drug, such as Vaponefrin,* prior to postural drainage was studied to determine its effect on the elimination of bronchographic media. Postural drainage was routinely performed three times on the day of bronchography and again the following morning. Residual oil remaining in the lungs after 72 hours following bronchograms with Dionosil Oily was determined roentgenographically by substituting iodinated peanut oil for the plain peanut oil in this medium. The use of the bronchodilator drugs after installations of Visciodol produce an 18 per cent reduction in the number of patients having significant amounts of residual oil in the lungs. The bronchodilator

*Vaponefrin used in this study was donated by the Vaponefrin Company, Upper Darby, Pennsylvania.

drugs had a similar reducing effect on the residual oil following Dionosil Oily installations. Of further interest is the fact that the opaque oil remaining in the lungs after Visciodol is less than the non-opaque oil following bronchography with Dionosil Oily (Figure 3).

PART II

Interpretation of Bronchographic Lesions

The fact that the findings on histological examination are not always consistent with the clinical opinion has necessitated a better method of clinico-pathologic correlation of areas with bronchial disease. Bronchiectasis has been studied previously by obtaining corrosion specimens; however, this prevents histological examination of the same areas. Others have studied bronchographic lesions by injecting the surgical specimen with opaque media and have taken roentgenograms of the injected specimens. This method allows the correlation of a bronchogram with the surgical specimen but it is often difficult to accurately localize a bronchial lesion for histological examination. If the surgical specimen is injected under controlled pressure with an opaque medium which solidifies during formalin fixation of the specimen, the segmental planes can then be dissected prior to roentgenographic study. The bronchus more nearly maintains its original size so the roentgenograms can be correlated segment by segment with the bronchogram for accurate localization of bronchial lesions (Figure 4). A medium now used for injection studies of this type

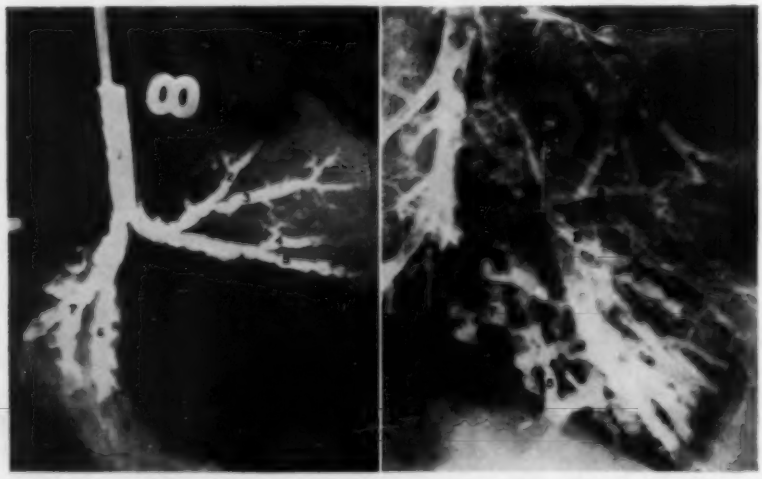

FIGURE 4A FIGURE 4B

Figure 4: Bronchogram and Injected Surgical Specimen. After left lower lobectomy, each segment is injected with an opaque medium which solidifies during formalin fixation. The segments are then separated and a roentgenogram made. This allows localization of bronchial defects for histological examination. The anteromedial basal segment (*A*) is compared with the lateral view of the preoperative bronchogram (*B*). The numbers on the bronchial branches correspond in each of the two illustrations. Only by this method could the location of such a defect be positively identified.

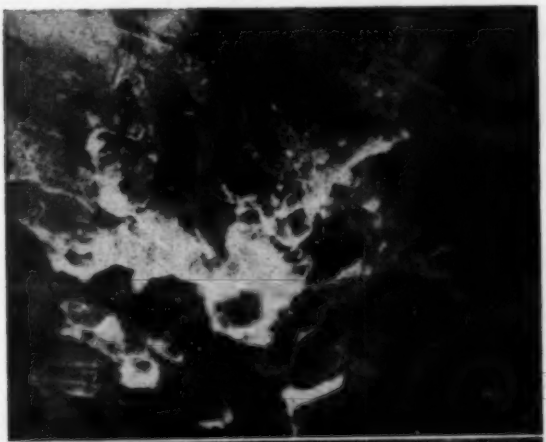

FIG. 5A

FIG. 5B

Figure 5: Inspiration and Expiration Bronchograms Showing Variation in Size of Saccular Tuberculous Bronchiectasis. Variation in size of saccular bronchiectasis in the right upper lobe is seen on lateral bronchogram in (*A*) inspiration and (*B*) expiration. A histological section from the posterior segmental bronchi is seen in Figure 6.

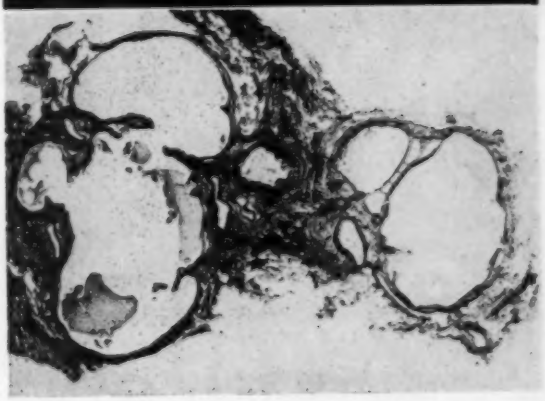

FIGURE 6: *Histology of Saccular Bronchiectasis Which Changes in Size During Respiration.* A thin layer of fibrous tissue and smooth muscle surrounds the dilated bronchi. Blood vessels are surrounded by greater amount of fibrosis. No active inflammatory reaction is seen. Massen Stain, 4x.

is made by mixing Lipiodol, egg yolk and acacia in appropriate amounts for the desired consistency. Studies of this nature increase the diagnostic potentialities of bronchial defects so adequate treatment can be made more effective.

Normal variation in the caliber of the bronchi can be observed on bronchograms taken during inspiration and expiration. Bronchi which show saccular dilatation (Figure 5) on inspiration but are markedly reduced in size during expiration usually show little or no evidence of inflammatory

FIG. 7A

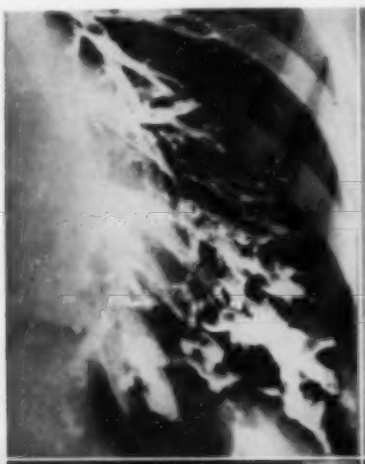

FIG. 7B

FIG. 8A

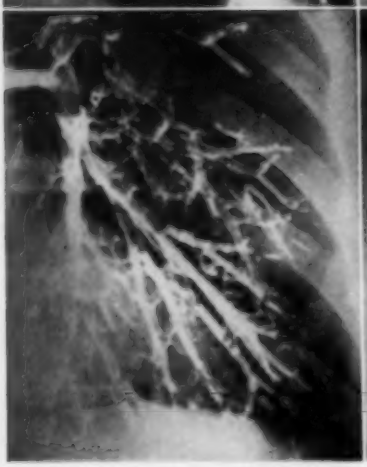

FIG. 8B

Figure 7: Outline of Bronchi in Areas of Bronchiectasis on 24-Hour Roentgenogram. (*A*) Bronchiectasis in left lower lobe is seen on bronchogram. (*B*) An outline of the bronchiectatic bronchi still present on the 24-hour roentgenogram shows evidence of poor bronchial cleansing.—*Figure 8: Normal Left Bronchogram with 24-Hour Bronchial Outline.* (*A*) Bronchogram left lower lobe shows normal outlines of bronchi. (*B*) Roentgenogram in 24 hours shows outline of two basal segments. Histological sections of one of these bronchi are seen in Figure 9.

reaction or fibrosis on histological examination (Figure 6). Bronchi which do not vary in size during the two phases of respiration more frequently show inflammatory changes or significant amounts of fibrous tissue in the bronchial wall. Roentgenograms are routinely taken in one view during the two respiratory phases in order to correlate these findings with histological sections.

Histological findings in early chronic bronchitis[6] consist of hypertrophy of the mucous-secreting elements which is corroborated by an excess of

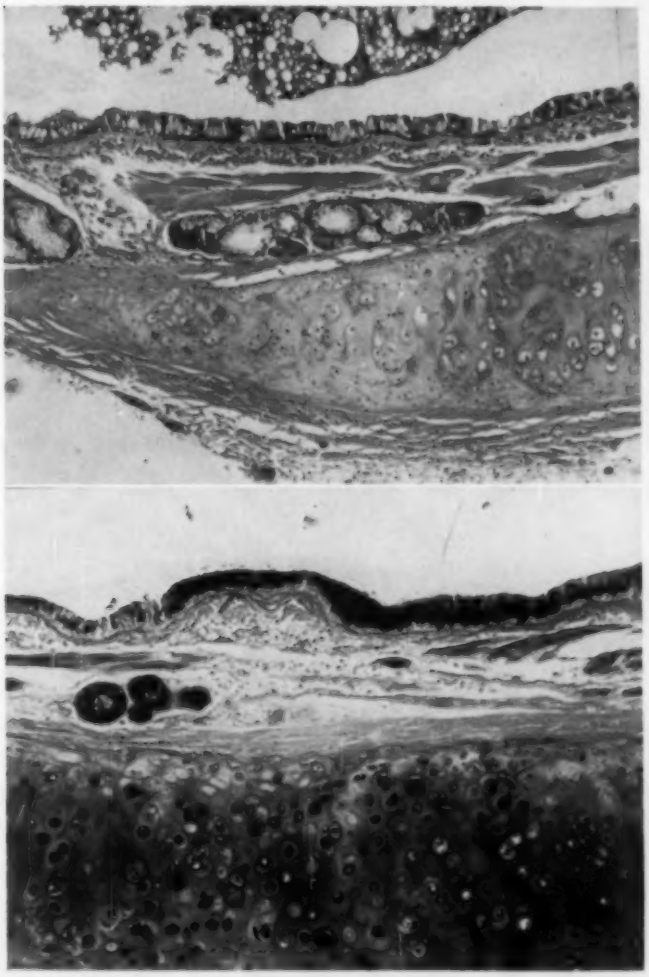

FIGURE 9A

FIGURE 9B

Figure 9: Histology of Bronchus Showing 24-Hour Outline. The basal bronchus outlined on the 24-hour roentgenogram in Figure 8B shows numerous goblet cells in the epithelium. (*A*) Hematoxylin and Eosin stain. (*B*) Periodic acid-Schiff stain is more specific for mucus. (67x)

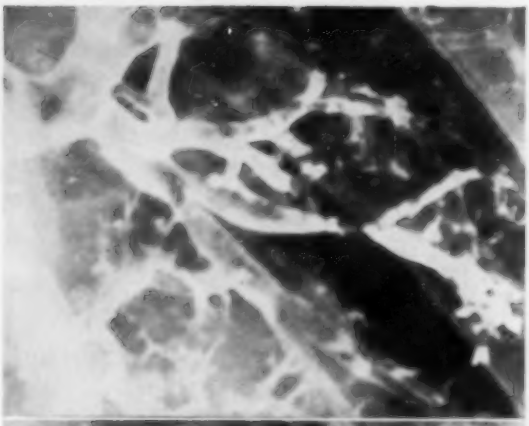

FIG. 10A

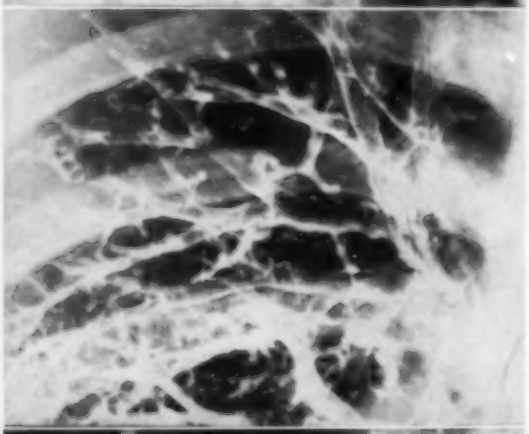

FIG. 10B

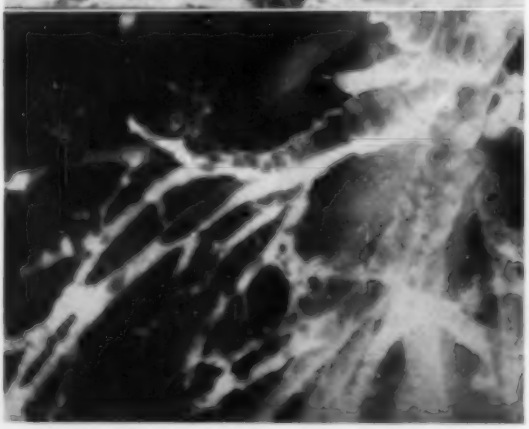

Figure 10: Bronchographic Changes in Early Chronic Bronchitis. (*A*) Wavy outlines of lingular bronchi; (*B*) Rippled appearance of the right upper lobe bronchi and (*C*) Transverse striations in the right middle lobe and basal segmental bronchi.

FIG. 10C

mucus in the air passages. These changes consist of an increase in the number of goblet cells in the epithelial surface and hypertrophy of the mucous glands with marked dilatation of their ducts. When an excess of mucus is present in the bronchi, the cilia exert little more than a churning action[7] on the mucus which steadily accumulates in the lungs requiring cough for evacuation. The resistance-lowering action of mucus together with purulent bronchiolitis and its sequela lead to progressive obliteration of pulmonary tissue thus setting the stage for production of emphysema.[6] In order to treat chronic bronchitis and prevent the progressive changes in the lungs, a definite diagnosis must be made in the early stage of this disease.

Outlines of the bronchial tree with bronchographic medium as seen on a subsequent roentgenogram (Figure 7) have been observed in the areas of bronchiectasis since the early days of bronchography. This has been attributed to a poor cleansing mechanism of the diseased bronchi. In chronic bronchitis one of the earliest changes which occurs in the bronchus is an impaired cleansing ability. This is apparent in a bronchus which appears normal on the bronchogram (Figure 8) but remains outlined on a roentgenogram in 24 hours. The only changes on histological examination of this bronchus (Figure 9) is an increase in goblet cells in the epithelium and a few inflammatory cells in the submucosa. A roentgenogram taken 24 hours after bronchography is extremely valuable to observe this cleansing mechanism. When bronchial outlines are observed, a closer examination of the bronchogram will frequently reveal less obvious structural changes in the walls of these bronchi.

In 1949 DiRienzo[5] and in 1953 Simon and Galbraith[9] have described

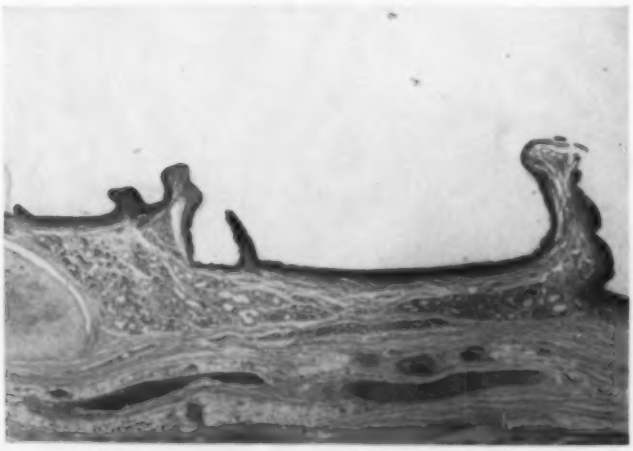

FIGURE 11: *Transverse Striations of Bronchial Mucosa In Chronic Bronchitis.* Longitudinal histological section (H&E Stain) of a bronchus shows transverse striations of the bronchial mucosa. Presence of inflammatory cells in the submucosa are consistent with a diagnosis of chronic bronchitis. The mucosal projections sometimes contain small bundles of smooth muscle.

some of the bronchographic findings in patients having chronic bronchitis. The use of Visciodol permits a more detailed study of these lesions so that a diagnosis can be made before more advanced changes occur. Bronchographic changes in early chronic bronchitis may consist either of wavy

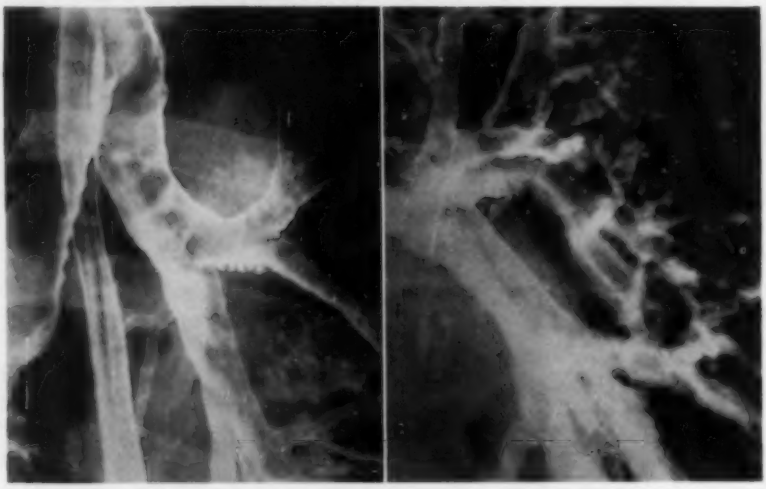

FIGURE 12A FIGURE 12B

Figure 12: Bronchographic Changes in Chronic Bronchitis Producing Diverticula. (*A*) Bronchial diverticulae seen in patients with chronic bronchitis may present a "saw-toothed" appearance, or (*B*) they may be so numerous that they produce "feathering" of the bronchial outline.

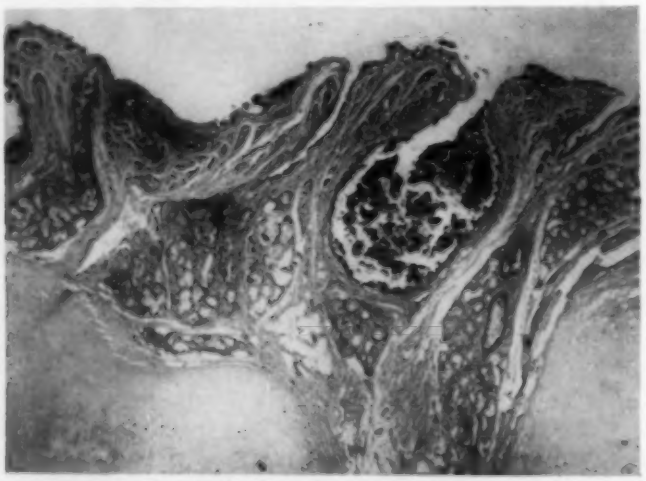

FIGURE 13: *Histology of Diverticula.* Two large dilated ducts of mucous glands are seen containing blood. Portions of three other ducts are seen with less evidence of dilatation. Hypertrophy of the mucous glands is evident.

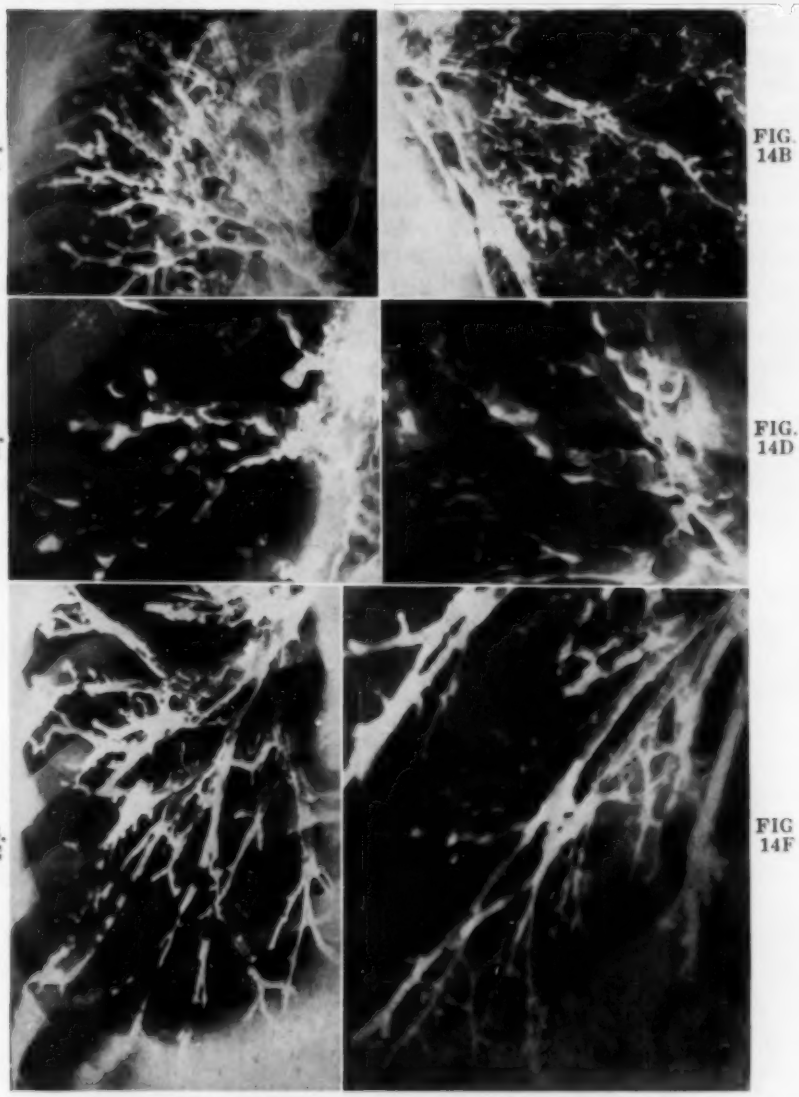

Figure 14: Bronchographic Changes in Advanced Chronic Bronchitis. (*A*) Cylindrical bronchiolectasis is evident in the right upper lobe when dilated bronchi approach the lung periphery; (*B*) Cystic bronchiolectasis is present in the left anterior segment; (*C*) Cylindrical and cystic bronchiectasis is present in a right upper lobe bronchus; (*D*) Diverticula are seen in a right upper lobe bronchus; (*E*) Areas of constriction and dilatation are seen in the right basal segments of a patient with secondary emphysema, and (*F*) "Pipe-stem" deformity of a right basal segmental bronchus is characterized by very little diminution in size of the bronchus.

outlines of the bronchi showing alternate areas of dilatation and constriction or of a rippled appearance (Figure 10). These areas of constriction and dilatation may vary in length and diameter. When the interval between them is small, transverse striations in the bronchial mucosa are prominent (Figures 10 and 11).

Associated with chronic bronchitis, one will occasionally notice small diverticula along the surface of the larger bronchi measuring up to three millimeters in diameter. These diverticula may be few or numerous. They may have the appearance of feathering along the edge of the bronchial wall or may have a saw-toothed appearance (Figure 12). Bronchial diverticulosis was first described by Morlock and Pinchin[10] in 1933, but it was not until 1953 that Duprez and Mampuys[11] showed that these diverticula were dilated ducts of the bronchial mucous glands (Figure 13). Irregularity of the transverse striations will occasionally show filling defects which simulate diverticula in the bronchogram.

Bronchographic lesions become more prominent (Figure 14) in later stages of chronic bronchitis. Bronchioles in the periphery of the lung

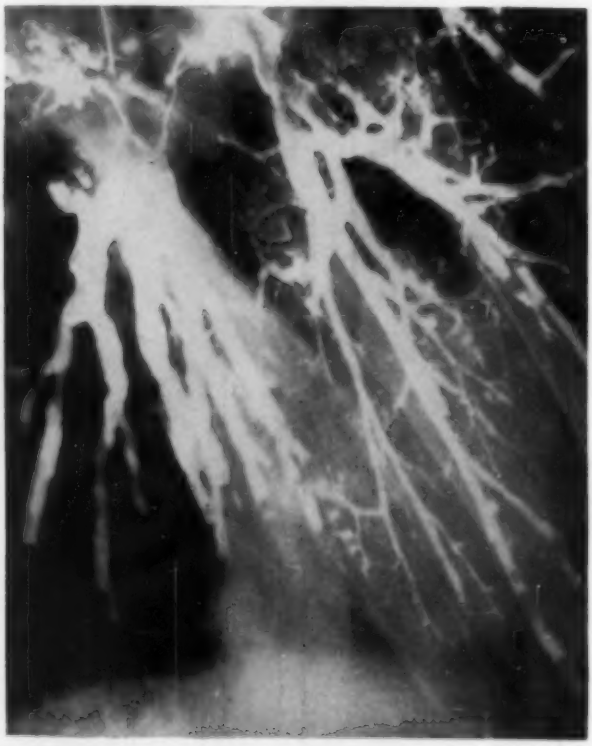

FIGURE 15: *Bronchographic Changes in Bronchitis Which Simulate Bronchiectasis.* An acute respiratory infection in a patient with chronic bronchitis produces changes in the basal segments of the left lower lobe which simulate bronchiectasis. Histological section of the posterior basal bronchus is seen in Figure 16.

may become dilated and show cylindrical or cystic bronchiolectasis. Medium sized bronchi may also show similar cylindrical and cystic dilatations. Cystic dilatations are due to destruction of the wall by localized areas of acute inflammation. Diverticula may appear along the walls of the medium sized bronchi. After the clinical symptoms of emphysema begin to appear, the basal bronchi may show areas having marked constriction of the lumen with distal dilatations or they may extend some distance without variation in the caliber of the lumen.

Bronchitis following an acute respiratory infection may produce such severe changes that a diagnosis of bronchiectasis is frequently made. This change was demonstrated by Blades[12] in patients with so-called atypical pneumonia. More often this is seen in patients with chronic bronchitis due to superimposed acute infection (Figure 15). On histological examination the bronchi show acute suppurative bronchitis (Figure 16). Bronchographic changes in acute bronchitis may be differentiated from those seen in true bronchiectasis by their symmetrical areas of dilatation and constriction, by relatively slight variation in the diameter of the bronchi and frequently by changes in other bronchi consistent with chronic bronchitis. Bronchial deformity produced primarily by atelectasis gives a similar appearance except the lumen decreases in diameter more rapidly due to relaxation and relative shortening of the bronchus. The nature of sputum

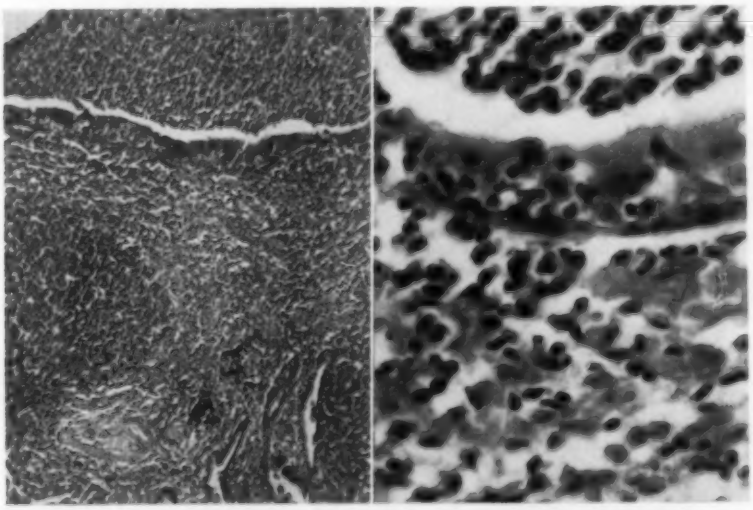

FIGURE 16A FIGURE 16B

Figure 16: Histology of Acute Bronchitis. Histological section of the posterior basal bronchus of the left lower lobe seen in Figure 15 shows acute suppurative bronchitis without fibrosis. (*A*) Acute and chronic inflammatory cells are seen in the bronchial wall and lumen. A lymph follicle is also seen (80x). (*B*) The epithelial layer is infiltrated with similar inflammatory cells. The smooth muscle fibers are separated by edema. There is no evidence of fibrosis or destruction of the bronchial wall to suggest bronchiectasis.

and the bronchoscopic findings are often helpful in differentiating these bronchial lesions.

A poor prognosis can be anticipated if we attempt to cure patients with chronic bronchitis by surgical excision of the more involved areas, unless we use intensive medical therapy during the immediate preoperative and postoperative periods. Following surgery these patients must continue indefinitely under good medical management. Some patients who receive adequate medical treatment may not require surgery (Figure 17). It is imperative that a bronchogram be inspected closely especially to observe the less obvious changes which are consistent with chronic bronchitis prior to surgical treatment.

CONCLUSIONS

1. Since all bronchographic media remaining in the alveoli may produce foreign body reaction, it is recommended that a technique of bronchography and a type of bronchographic medium be used in which alveolar filling is not seen. There is less alveolar retention after Visciodol than after other bronchographic media.

2. The technique of selective bronchography using the Metras catheters is of value when there is insufficient outlining of a particular segment during a previous bronchographic examination. Routine bronchography in selected cases using an appropriate Metras catheter prevents the necessity of repeated bronchograms.

3. A method for correlating bronchiographic defects with their histo-

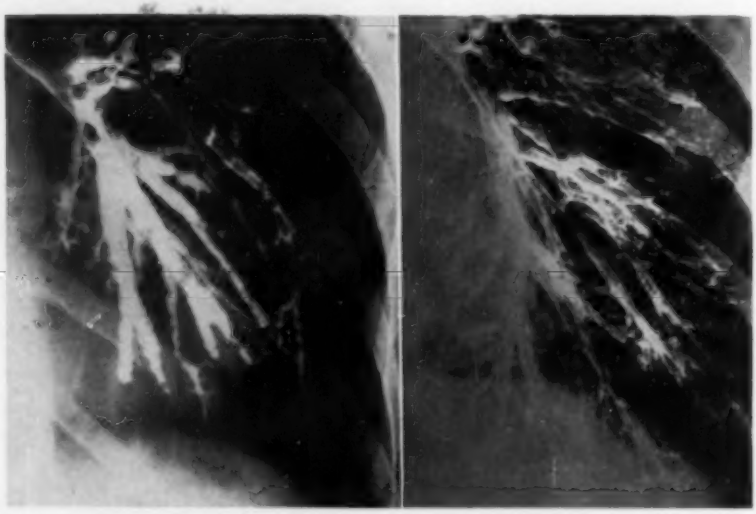

FIGURE 17A FIGURE 17B

Figure 17: Results of Conservative Treatment of Acute Bronchitis. (*A*) Changes in the bronchial outlines in the left basal segments in a patient with acute bronchitis simulate bronchiectasis. (*B*) Conservative treatment resulted in reversal of these changes as can be noted in a repeated bronchogram three weeks later.

logical appearance has been described. We believe that this study will increase our knowledge of the significance of these defects.

4. A roentgenogram made 24 hours after bronchography should become a part of the routine bronchographic procedure so that our attention can be directed to less obviously involved areas of bronchial disease. Roentgenologists should be encouraged to include this in the total cost of the bronchogram.

5. Bronchography using Visciodol has made possible a more detailed study of bronchial defects. Bronchographic findings in acute as well as various stages of chronic bronchitis are described. In order to give proper treatment to patients with acute or chronic bronchitis, these less obvious lesions must be recognized on bronchography.

RESUMEN

1. Puesto que todos los medios de contraste para broncografía producen reacción de cuerpo extraño cuando permanecen en los alveolos, se recomienda que se adopte una técnica de broncografía con un medio que no permita el llenado alveolar. Hay menos retención alveolar después de usar Visciodol que después de otros medios.

2. La técnica de la broncografía selectiva con las sondas de Metras es de valor cuando hay insuficiente delimitación de algún segmento en particular según se haya visto en broncografía previa. La broncografía de rutina en casos adecuados usando una sonda de Metras evita la necesidad de repetir los broncogramas.

3. Se describe un método para correlacionar los defectos broncográficos con su apariencia histológica. Creemos que este estudio aumentará nuestro conocimiento de la significación de estos defectos.

4. Un roentgenograma hecho 24 horas después de broncografía debe formar parte del procedimiento broncográfico de modo que nuestra atención se enfoque a las áreas menos comprometidas por la enfermedad bronquial. Los radiólogos deben animarse a incluir esto en el costo total del broncograma.

5. La broncografía con Visciodol hace posible un estudio más detallado de los defectos bronquiales. Se describen los hallazgos broncográficos en casos agudos o de bronquitis crónica. Para dar tratamiento adecuado a los enfermos con bronquitis aguda estas lesiones menos aparentes deben ser reconocidas por la broncografía.

RESUME

1. Puisque tous les produits utilisés pour la bronchographie qui stagnent dans les alvéoles peuvent se comporter comme des corps étrangers, les auteurs recommandent d'employer une technique de bronchographie et un type de produit avec lesquels on ne voie pas le remplissage alvéolaire. La rétention alvéolaire est moindre après usage de "Visciodol" qu'après tout autre produit à usage bronchographique.

2. La technique de bronchographie sélective utilisant les cathéters de Metras est de grande val eur quand le dessin d'un segment particulier s'est

montré insuffisant au cours d'un examen bronchographique préliminaire. Une bronchographie de routine, dans des cas choisis, utilisant le cathéter de Metras, évite la nécessité de bronchogrammes répétés.

3. Les auteurs décrivent une méthode qui met en parallèle les altérations bronchographiques à leur traduction histologique. Ils pensent que cette étude augmentera nos connais sances sur la signification de ces altérations.

4. Un cliché radiologique 24 heures après la bronchographie devrait faire partie de la technique bronchographique de routine, de telle sorte que l'attention puisse être dirigée sur des zones bronchiques dont l'atteinte est moins évidente. Les radiologistes devraient être encouragés à faire entrer cet examen dans le montant des frais de la bronchographie.

5. La bronchographie utilisant le visciodol a rendu possible une étude plus détaillée des altérations bronchiques. Les auteurs rapportent leurs constatations bronchographiques dans les bronchites aiguës et dans les différents stades des bronchites chroniques. Pour traiter comme il convient les malades atteints de bronchite chronique ou aiguë, il est nécessaire de reconnaitre sur la bronchographie des altérations qui apparaissent de façon moins évidente.

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Bronchography: Summary of a World-Wide Survey
Report of Committee on Broncho-Esophagology

The introduction of contrast media into the bronchial tree for diagnostic purposes was first performed by Sicard and Forestier[1] in 1922. Since then bronchography has been used throughout the world and is universally recognized as a valuable aid in the diagnosis of bronchopulmonary disease. Bronchograms are made by many physicians with very different professional backgrounds: radiologists, otolaryngologists, thoracic surgeons, specialists in pulmonary disease—all are involved in the making of roentgenograms of the bronchial tree. The committee on Broncho-esophagology of the American College of Chest Physicians felt that it would be worth while to make a survey of bronchography as it is used today. We were interested in types of media, technics, anesthesia, indications and contraindications, complications and fatalities. We were interested also in the problem of bronchography in children.

With these thoughts in mind, questionnaires were prepared and sent to 60 physicians who are interested in bronchography. Twenty radiologists, 20 otolaryngologists and broncho-esophagologists and 20 thoracic surgeons were chosen. The majority of these men practice their specialty in various parts of the United States. However, several Canadians were included, eight men from Europe, two from South America and one from Japan. The results of this survey have been recorded and will be presented herein.

Findings

Replies were received from 57 of the 60 men to whom questionnaires had been sent. In some instances, the recipient of the questionnaire passed it on to one of his colleagues in related fields who usually did the work. Thus, final replies were obtained from 22 radiologists, 21 thoracic surgeons and 14 laryngologists and bronchoscopists. In some areas bronchography was a co-operative venture between a radiologist on one hand and a thoracic specialist or otolaryngologist on the other. This was very often true in children in whom anesthesia was required, and the contrast medium was instilled through a bronchoscope or an endotracheal tube. If both bronchoscopy and bronchography were indicated, 25 specialists indicated that they performed both procedures on the same day with the same anesthesia, while 28 others almost always made a separate procedure of bronchography.

In preparation for bronchography, postural drainage was employed by more than half of the participants but was almost routine after the procedure. Aerosol bronchodilators were administered just before bronchography at times, and occasionally aerosol detergent preparations were used. Sedative medications of the barbiturate type were given to patients by 41 men, and 25 used atropine routinely for premedication. The use of opiate derivatives such as morphine, codeine, demerol and even heroin was advocated by 35 of the participants but was sharply criticized by many men. Nine thoracic surgeons gave drugs of the antihistaminic group prior

to instillation of the contrast medium. Premedication was not used by 12 men who responded to the questionnaire.

Local anesthesia was employed universally among adults. Cocaine and pontocaine were the favorite agents but several of the correspondents favored cyclaine, xylocaine or other surface anesthetics. Occasionally Forrester's solution, commonly used for bronchospirometry, was recommended (Table I). These agents not only were applied topically to the hypopharynx by many but also were instilled into the trachea and bronchi with the aid of a Luken's type syringe. All agreed that proper anesthesia was essential for good bronchograms.

The technic of instilling the contrast medium varied greatly, but the great majority of men expressed a preference for the catheter method. Nearly always, a No. 14 catheter was passed through one of the nostrils and then guided into the trachea. Ten of the 57 specialists still prefer supraglottic instillation, and one surgeon instills the medium into the hypopharynx through a nasal catheter. The transtracheal technic is employed by only three of our correspondents. Although this method has enjoyed considerable favor in Great Britain, it has been virtually abandoned by specialists in the United States because of the occasional complication that follows insertion of the needle through the tracheal wall.

The choice of contrast media was of special interest (Table II). Many of the men used one agent exclusively and were most emphatic in their preference. However, others used two or more preparations, and it was evident that they are still searching for the ideal substance for bronchography. A small but determined group of investigators employed an iodized oil thickened with sulfanilamide. They pointed out that alveolar filling is rare with thick Lipiodol but they do admit that the procedure is very time consuming. Oily Dionosil (propyliodone) is certainly the favorite preparation at the present time. The enthusiasm for aqueous dionosil seems to be waning, partly because the material is irritating and partly because of unfavorable reactions and even fatalities. In dionosil the iodine is in organic combination and there is no risk of iodism. Propyliodone (Cilag) is very similar to dionosil and appears to be a satisfactory medium, according to Swiss authorities. Umbradil viscous B is rarely used.

TABLE I
LOCAL ANESTHETIC AGENT USED FOR BRONCHOGRAPHY (57 REPLIES)*

Drug	Participants, Number
Tetracaine hydrochloride (pontocaine)	31
Cocaine	28
Lidocaine hydrochloride (xylocaine)	8
Hexylcaine hydrochloride (cyclaine)	7
Forrester's solution	2
Others	4

*Several participants listed two or more agents.

TABLE II
CONTRAST MEDIA USED FOR BRONCHOGRAPHY (57 REPLIES)*

Medium	Participants, Number
Oily dionosil	29
Aqueous dionosil	18
Lipiodol	15
Iodochloral	14
Lipiodol with sulfanilamide	3
Propyliodone (cilag)	1
Umbradil	1
Maljodal (Japanese)	1

*Several participants used two or more media.

The quantities of media used for bilateral bronchograms varied greatly. Forty-nine of the participants provided satisfactory replies to this question (Table III). It seemed obvious that a larger quantity was needed when oily Dionosil was used, but the larger amount was apparently well tolerated.

Only seven of the 57 participants stated that complete bronchography was not routine. Forty-four made bilateral bronchograms on the same day with the same anesthesia, while 13 specified that each side of the bronchial tree was filled separately on different days. Of the 50 physicians who answered the question regarding fluoroscopy 34 instilled the contrast medium with fluoroscopic guidance, while 16 did not use the fluoroscope.

The majority of bronchographers instilled media into the right side of the bronchial tree first and obtained films made in the anteroposterior, right posterior oblique and right lateral projections (Table IV). Then, either immediately or at a subsequent session, the left side was filled and anteroposterior and left posterior oblique views were made. A few men filled both sides of the bronchial tree before taking films and were content with anteroposterior and both oblique projections. In the majority of instances, four to six films (14 by 17 inches) were employed. Very few made stereoscopic films.

Spot films were used routinely by 12 correspondents, while others made spot films occasionally. The Metras catheters with the curved tip are particularly useful for selective bronchography. These were used to good

TABLE III
MEDIA FOR BILATERAL BRONCHOGRAPHY (49 REPLIES)*

Amount of Contrast Media, Cubic Centimeters	Participants, Number
Less than 20	4
20 to 25	13
30 (about)	17
40 (about)	15

*Eight participants did not answer this question.

TABLE IV
DATA ON ROENTGENOGRAPHY (57 REPLIES)

View	Number of Films	Number Who Used
Posteroanterior and both obliques	3	2
Posteroanterior, right lateral, both obliques	4 to 8	43
Posteroanterior, right lateral, both obliques, plus spot films	8 or more	12

advantage by several European and Canadian bronchographers. The majority, however, relied on various posturing technics in order to map out the various segments of the lung. The x-ray tilt table was rather useful for placing the patient in a variety of positions during and after instillation of medium. Most men agreed that accurate timing was desirable for optimal filling of the bronchial tree, while others relied on fluoroscopic control. Individual technics varied tremendously, and yet it was obvious that all of the correspondents were capable of obtaining satisfactory bronchograms.

All physicians who replied agreed that the demonstration and localization of bronchiectasis were by far the most important indication for lung mapping (Table V). There was considerable difference of opinion about the value of bronchograms in the diagnosis of bronchial tumors; the radiologists were rather enthusiastic about the method, while many of the broncho-esophagologists and surgeons felt that bronchograms were neither necessary nor desirable. A similar disagreement was evident regarding the value of bronchograms in tuberculosis. Many felt that radiopaque material should be instilled only if there was a strong clinical suggestion that bronchial disease accompanied tuberculosis. It was interesting to note that bronchography was seldom employed for the diagnosis of lung abscess but it was used very often in the evaluation of hemopty-

TABLE V
USE OF BRONCHOGRAPHY: INDICATIONS AND CONTRAINDICATIONS (57 REPLIES)

Condition Indicating Use	Participants Who Agreed	Condition Contra-indicating Use	Participants Who Agreed
Bronchiectasis	57	Iodine-sensitivity (history)	30
Indeterminate hemoptysis	50	Recent pneumonitis	26
Bronchostenosis	43	Heart disease	18
Bronchial tumors	38	Asthma	18
"Middle-lobe syndrome"	36	Emphysema	16
Chronic cough	23	Trauma (acute)	14
Tuberculosis	17	Tuberculosis (active)	12
Abscess of lung	4	Advancing age	11

sis of obscure origin. It was not used too frequently for the study of chronic coughs.

The principal contraindications to bronchography are listed in Table V. The committee was surprised that a greater number of physicians did not fear the introduction of opaque material in patients having diseases such as asthma, emphysema and heart disease, and in older people. A few who answered still feel that bronchography is hazardous in pulmonary tuberculosis, and a number of instances were cited in which dissemination of tuberculosis had resulted. Many feel that the risk of iodine sensitivity is greatly reduced if dionosil is used instead of iodized oil.

All participants described some complications but considered them rare (Table VI). Some of the untoward effects could be attributed to obstruction of the bronchi by the contrast material. Others were thought to be manifestations of iodine sensitivity. Four men use a skin test to check for iodine sensitivity, while two others give iodine orally for the same reason. All agreed that iodized oil in the stomach was the principal source of iodine reaction. Three men routinely lavaged the stomach, while one authority gave a cornstarch preparation following bronchography to absorb the iodine. Granuloma of the lung in resected specimens was described by 10 of our correspondents. It was noted after oily preparations were used but less frequently with aqueous preparations having a carboxymethyl cellulose base. The granulomatous reaction occurred especially after massive bronchial and alveolar filling. Several authorities still recommend that pulmonary resection be deferred for 3 to 4 weeks after a bronchogram has been made.

Seventeen fatalities were reported in connection with the making of bronchograms. Eight of these occurred after administration of local anesthetics but before any contrast medium was instilled. In the other nine, however, death occurred after the contrast substance was introduced

TABLE VI
COMPLICATIONS OF BRONCHOGRAPHY (57 REPLIES)* †

Complication	Number Who Had Encountered
Fever	29
Skin lesions	22
Facial edema	19
Asthma	19
Pneumonitis	16
Parotitis	15
Granuloma (removed specimens)	10
Pneumothorax	5
Dissemination of tuberculosis	4
Atelectasis	3

*Reactions to local anesthesia excluded.
†Incidence of complications estimated from 0.5 to 2 per cent.

(Table VII). It is estimated that the combined experience of our 57 collaborators probably represents a total of some 50,000 to 100,000 bronchograms. Hence, the mortality rate is very low, but bronchography is not without risk.

Part of our questionnaire was devoted to the problems of bronchography in children. Forty-eight of the 57 men reported experience with children (Table VIII). In small children general anesthesia was almost universally employed. A few authorities felt that satisfactory bronchograms could be obtained with local anesthesia or even no anesthesia. Ether was the agent of choice and was considered safest. Eleven men used pentothal

TABLE VII
DATA CONCERNING NINE FATALITIES OWING TO BRONCHOGRAPHY*

Case	Age Group	Contrast Medium	Cause of Death
1	Child	Aqueous dionosil	Anoxia; cystic lung disease
2	Child	Lipiodol	Anoxia; mucoviscidosis
3	Adult	Oily dionosil	Anoxia; bronchospasm
4	Adult	Oily dionosil	Anoxia; emphysema (excess sedation)
5	Adult	Aqueous dionosil	Anoxia; emphysema
6	Adult	Oily dionosil	Anoxia; bronchospasm (bronchiogenic cancer)
7	Adult	Lipiodol	Iodine sensitivity, with bullous skin lesions
8	Adult	Iodochloral	Dissemination of tuberculosis
9	Adult	Oily dionosil	Cardiac arrest

*Combined experience of all 57 physicians who replied.

TABLE VIII
BRONCHOGRAPHY IN CHILDREN (48 REPLIES)*

Anesthesia: Type, Agent, Route	Participants, Number
Anesthesia:	
Local	8
Local with tribromoethanol (avertin) given rectally	3
Ether	34
Thiopental sodium (pentothal) given intravenously	11
Nitrous oxide	1
Method or route of introduction:	
Bronchoscope	11
Catheter	31
Endotracheal tube	6
Transglottic	2

*Some men did not do bronchography in children; others used more than one method.

sodium intravenously and most of these used a technic employing both an intratracheal tube and a catheter. Avertin, given rectally, and nitrous oxide were used rarely. The medium was instilled via a catheter by 31 men, via the bronchoscope by 11, through an endotracheal tube by six, and by injection through the anterior wall of the trachea by two participants. The same types of media were used for children, but about half of the quantity used for adults was instilled. Indications for bronchography are much the same in children and adults, but the method can be used for the diagnosis of cystic disease of the lung, tracheo-esophageal fistula, congenital anomalies and also for the pulmonary manifestations of fibrocystic disease of the pancreas.

Contraindications to bronchography in children are similar to those in adults. However, certain hazards in the performance of bronchography in infants and children must be borne in mind. In addition to the risks of general anesthesia, the possibility of laryngeal edema also must be considered. Furthermore, the presence of large amounts of contrast media in the bronchial tree may produce asphyxia and in some instances has been responsible for death.

In general, the majority of men were of the opinion that bronchography in children was reliable. However, 12 of them felt that interpretation of the bronchograms in children was difficult and that it often was not easy to interpret the extent of the disease. Some of the thoracic surgeons were particularly concerned about the reliability of bronchography in children.

All of the participants were asked whether bronchography was being employed to a greater or lesser extent in their practice. About two thirds of those who answered the question felt that bronchography was being used with increased frequency. Although less bronchiectasis was encountered, the procedure was used oftener for investigation of hemoptysis, bronchostenosis and chronic cough than for bronchial tumors and tuberculosis. In evaluation of bronchial obstruction and cavitation, tomography is replacing bronchography as a radiographic technic.

Comment

The Committee on Broncho-esophagology realizes that the participants in this questionnaire were a selected group and that, therefore, the opinions expressed may not be representative. Nevertheless, many of the men who were contacted are considered authorities on bronchography and many of them have published articles on this method of examination. As previously stated, it has been estimated that the combined experience of the group would probably total between 50,000 and 100,000 bronchographic examinations. The committee is very grateful to the participants for the fine cooperation shown in this project. In addition to completing the questionnaire, a number of the men wrote lengthy letters with discussions of various points, and a number sent reprints which reflected their experience.

CONCLUSIONS

The participants in this study and the members of the Committee on Broncho-esophagology consider bronchography to be an important diagnostic aid. Bronchography should be done by physicians with training and experience who are willing to take the time to do it well. It should not be delegated to the inexperienced intern or resident. Too often bronchography is treated as a "stepchild." If bronchography is worth doing at all, it should be done well.

No longer do we think of bronchography as merely a means of confirming a diagnosis of bronchiectasis already suspected or as a roentgenoscopic demonstration of an obstruction already seen through the bronchoscope. Today the thoracic surgeon requests precise information as to the segments involved in bronchiectasis of tuberculosis, and above all he wants to know which bronchi are normal. In segmental resection of the lung the results may be disastrous if this information is not available to the surgeon. Thus complete bilateral bronchography is essential.

Even the most experienced bronchographer does not claim more than 90 per cent success in obtaining adequate bronchograms, and in less capable hands the number of poor bronchograms is considerable. Hence, it is obvious that there is plenty of room for improvement in the technic of bronchography. Good anesthesia is essential but the agent must be administered within the limits of safety. We are still searching for the perfect contrast medium and present technics can certainly be improved. Bronchography in children deserves particular attention, both with respect to selection of patients and to performance of the procedure. Of prime importance is the maintenance of an airway for the administration of oxygen. At present it would seem that both an intratracheal tube and a catheter should be passed into the trachea so that oxygen can be given before, during and after the instillation of the contrast substance.

Interpretation of bronchograms requires a thorough knowledge of bronchial anatomy and the common bronchial variations. Considerable experience is essential for the reading of bronchograms, and interpretation should be correlated with the clinical problem as well as other roentgenographic studies of the thorax. Bronchospasm, retained secretions and recent pneumonitis or atelectasis may profoundly alter the bronchographic pattern. Too often an opinion is expressed on an inadequate bronchogram.

Much remains to be learned about the physiology of the bronchial tree. A good deal of information can be obtained by motion pictures of the fluoroscopic image of the bronchial tree filled with contrast medium. Up to the time of this report such technics have been impractical because of the radiation hazard. It is hoped that with improvements in image-amplifier equipment, the bronchial tree can be studied in action. Hence, it is possible that bronchography will make a contribution to our knowledge of pulmonary physiology as it already has to bronchial anatomy.

Committee on Broncho-esophagology

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REFERENCE

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Discussion

SHELDON E. DOMM, M.D., F.C.C.P.

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Of the many points raised by these two excellent papers there should be no question regarding one statement from the first presentation, "All of the men who participated in this questionnaire agree that bronchography is an important diagnostic aid and that it certainly should not be treated as a stepchild." It is refreshing to hear this after reading a recent paper from which one gets the impression that at one institution bronchograms apparently are made and interpreted by the junior residents.

The Committee on Bronchoesophagology of the College is to be commended for making this timely survey of bronchography. And the Program Committee deserves credit for including this subject on the program, and for selecting Dr. Rayl and Dr. Smith to give the findings of the extensive and dedicated studies they and their associates are making at Oteen.

I am sure all of us in this room who are doing bronchography could take issue with many of the details presented by the two essayists. It is well, however, to repeat the wise observation of Dr. Olsen that "individual techniques vary tremendously, yet it is obvious that all the correspondents are capable of obtaining satisfactory bronchograms."

In this connection it might be mentioned that there is a tendency toward oversimplification inherent in the questionnaire approach. This is shown by the fact that a number of the men wrote lengthy letters in addition to completing the questionnaire, and also by the fact that in many of the categories some men listed more than one technique or material.

Nevertheless a sufficient number of controversial points remain to provide heated argument on every one of the 18 questions. For example only

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half of the participants use postural drainage in preparation for bronchography. This should be routine. The questionnaire did not make clear how many men believe in doing diagnostic (and possibly therapeutic) bronchoscopy some days or weeks prior to bronchography. We believe this should be routine with few exceptions.

I was interested to see that the majority fill the right side first, presumably regardless of the location of the lesion. This habit seems no more logical than the practice of one man I know who always fills the left side first simply because it is harder to fill. We believe the more involved side should be mapped first so that a true lateral film, certainly the most valuable view for the surgeon, can be obtained.

The alleged disagreement regarding the value of bronchography in tuberculosis may simply reflect Dr. Olsen's observation that "our correspondents are not working much with T.B." It is my understanding that preoperative bronchography is routine in most tuberculosis centers at the present time, and my opinion that it should be.

I was glad to see waning enthusiasm for aqueous Dionosil, and equally glad to note that Oily Dionosil is the favorite preparation at this time. In this connection Dr. Rayl's experiment showing retention of the peanut oil in spite of the disappearance of the radiopaque propyliodone is of great interest from the pathological point of view. The experience of most men, however, seems to be that Dionosil Oily does not foul up one's subsequent x-ray series by virtue of alveolar retention insofar as x-ray interpretation is concerned. This is the crux of the Dionosil-Visciodol controversy. One notes that Dr. Rayl reports an 18 per cent reduction in the per cent of objectionable alveolar retention following Visciodol instillation, by the use of Vaponephrin bronchodilatation. This gives a figure of 6 per cent retention as compared to an earlier estimate of 15 per cent (without Vaponephrin). These figures, reflecting our experience, seem unacceptably high. We would not use Visciodol in a case in which alveolar retention of radiopaque medium must be avoided.

Dr. Rayl and Dr. Smith have made a nice contribution in the development of a technique of injecting surgical specimens with an opaque medium which solidifies. They should be commended also for stressing the importance of bronchitis in any consideration of bronchography and bronchiectasis; this is a most neglected and most important subject. We also believe in the value of a routine x-ray film a day or two following bronchography, having made some interesting diagnoses by this simple device.

Not knowing whether Dr. Henry Houghton of South Africa had been polled by Dr. Olsen I wrote to Dr. Houghton who, as you know, reported in 1953 a series of 7,000 bronchograms using Lipiodol thickened with Sulfanilamide, inquiring whether he is still enthusiastic regarding its use. Dr. Rayl will be encouraged to know that the "small but determined group" of Visciodol advocates referred to by Dr. Olsen still has a champion in Dr. Houghton who is "well satisfied with Visciodol."

Sheldon E. Domm, M.D.

A Preliminary Report on the Safety and Therapeutic Activity of a Salizid INH Derivative

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Although the development of INH greatly advanced the chemotherapy of pulmonary tuberculosis, there are many cases that still cannot be controlled adequately. As a consequence there is a continued search for agents which might provide greater inhibition of the tubercle bacillus with even less toxicity for man. Among the newer of the hydrazine derivatives is salicylidene hydrazine (Salizid® Nepera). This report covers our preliminary investigation of the toxicity, and the therapeutic activity of this compound.

Salizid is obtained from the interaction of the isonicotinic acid hydrazide and salicylaldehyde. It is sparingly soluble in the ordinary solvents and does not lose its inhibitory activity against *myobacterium* upon autoclaving for two hours at 20 pounds pressure. The difference in chemical structure between INH and Salazid is shown in Figure 1.

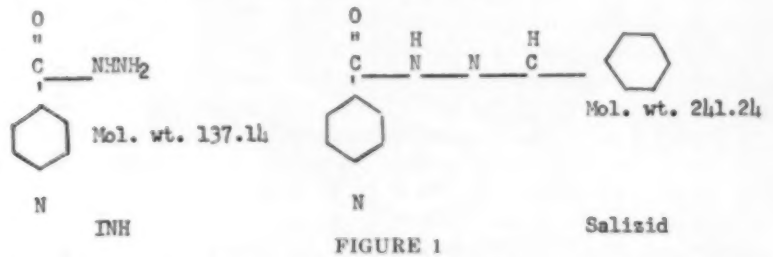

FIGURE 1

Hart[1] et al first reported that Salizid was strongly inhibitory against H=R. *in vitro*. Resistant H=R. cultures were found to die out in a few passages and organisms resistant to several other antituberculosis compounds were found, *in vitro*, to be sensitive to this compound. Steenken[2] et al, however, found that Salizid retained only a slight degree of inhibitory activity against the resistant H=R. strain. This *in vitro* finding was substantiated by animal studies as only a few of the guinea pigs inoculated with INH resistant strain responded better to Salizid than to INH and other INH derivatives. Both of these authors suggested that Salizid merited thorough clinical study, particularly in INH sensitive disease.

In early clinical trials, McCormick[3] et al reported that Salizid was well tolerated in large doses and that a majority of the patients who develop peripheral neuritis as a result of INH therapy may be treated safely with this agent. The response in 50 original treatment patients was prompt and excellent in 41, delayed, but good in four, symptomatic improvement

From the Medical Service, Veterans Administration Hospital.

TABLE I
E.E.G.

	Dec.	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	
P. W.	N 0 mgm			N 400 mgm		N 800 mgm			N 1200 mgm			
J. Y.			M. A. 0 mgm	0					? 800 mgm		N 800 mgm	Improvement on serial study
S. R.	M. A. 0 mgm			M. A. 400 mgm							M. A. 800 mgm	No change on serial study
E. H.	N 0 mgm			N 400 mgm		N 800 mgm			Surgery dropped from study			
J. E.	N 0 mgm		Too weak for further testing									
M. G.		M. A. 0 mgm		M. A. 400 mgm		M. A. 800 mgm			N 1200 mgm		M. A. 1200 mgm	No change on serial study
A. S.	N 0 mgm			N 400 mgm		N 1200 mgm			N 1200 mgm		N 1200 mgm	No change on serial study

N—Normal

M. A.—Mildly and moderately abnormal

"mgm" refers to mgm. of Salizid per day at the time of the E.E.G.

with only slight roentgenographic improvement in two, and three deaths. Ewart and Wingo[4] also reported that this compound was safe in doses of at least 1200 mgm. per day. These investigators found that INH resistant cases at 300 mgm. per day were not benefited by larger doses of Salizid. Recently, Nagley[5] reported that Salizid was an excellent and safe agent for the treatment of pulmonary tuberculosis and that in human beings, resistance was not built up as quickly to Salizid as to INH.

In our preliminary investigations, in 18 tuberculous men we attempted to determine the toxicity of this compound and its therapeutic value in: a) cases of peripheralneuritis, b) SM-PAS failures, c) seriously ill cases of pulmonary tuberculosis, d) INH resistant cases.

1) *Toxicity Evaluation.*—This part of our evaluation was carried out in seven colored men 25 to 65 years of age. All of these had a history of multiple admissions for chronic, far advanced active pulmonary tuberculosis. All had failed to respond to SM-PAS therapy, and had shown all clinical and laboratory evidence of being resistant to INH. Salizid was given for a minimal period of eight months and a maximum of 22 months.

The average dosage received by this group is summarized as follows:

4 months on 400 mgms. a day
5 months on 800 mgms. a day
6 months on 1200 mgms. a day

and in addition two other patients received 1600 mgm. daily for 10 months.

All were studied for possible neurotoxicity and hepatoxicity:

a) Neurotoxicity—there was no objective evidence of neurotoxicity. There was no euphoria or nervousness. In all, 23 electroencephalograms were carried out on six patients, and no abnormality was initiated or aggravated in any. The data for an 11 month period during the study is shown in Table I. Serial study gave the impression that there was a serial slowing of the pattern. This slowing was greater than one could expect from six unselected patients; but nevertheless was not enough of a slowing to be considered abnormal in any one of the cases studied.

b) Liver toxicity—no case was discontinued and no dosage reduced because of toxicity. A battery of liver function tests were performed at two week intervals during the first two months. After the second month, the tests were reduced to monthly determinations of serum bilirubin, thymol turbidity, cephalin flocculation and B.S.P. retention. Thymol turbidity, cephalin flocculation, cholesterol, prothrombin time, alkaline phosphatase and cholesterol esters, produced a number of minor variations similar to previous values on these and similar patients on INH therapy. Direct, indirect and total serum bilirubin demonstrated no abnormality on approximately 200 determinations.

The bromsulfalein excretion tests were more difficult to interpret. The three most severely ill patients had a scattering of B. S. P. retention values ranging from 10 to 25 per cent. They demonstrated no consistent pattern. There was no liver damage demonstrated when they were examined at post-mortem and the mode of death did not suggest liver toxicity.

The individual cases are summarized in Table II. Only one case (A. S.)

TABLE II

SUMMARY OF TOXICITY STUDY

Patients Name	400 mg.	800 mg.	1200 mg.	1600 mg.	Final Disposition	Change	Function Liver Findings	E. E. G.	P. M. Findings
J. E.	3 mo.	8 mo.	1 mo.		Death—Heart failure	Not evaluated because of edema	Normal	Not done too weak	Liver normal
M. G.	10	3	5	4 mo.	Death—Advanced Tbc.	—8 pounds possible due to edema	Normal	No change, on serial study	Liver normal
S. R.	3	8	10		Lobectomy	—4 pounds	Normal	No change, on serial study	
A. S.	3	3	7		Death—Advanced Tbc. & empyema	—10 pounds progressive empyema	Serial BSP, abnormal	No change, on serial study	Liver normal
P. W.	3	3	5	10	No change in Tbc. at end of study	No change	Normal	No change, on serial study	
J. Y.	3	5	6		No change	No change	Normal	Improvement on serial study	
E. H.	4	4			No change	+5 pounds	Normal	Dropped from study	

showed any abnormal change in liver function (B. S. P.) during the entire study which might have indicated possible liver damage. On postmortem examination the liver showed no evidence of toxic changes.

Effect in Cases with Peripheral Neuritis

Salizid was administered to a total of seven tuberculous patients, whom we desired to treat with INH, but who had various neurological disorders. The dosage of Salizid for these cases was 300 mgm. a day, a dosage equivalent to the routine dose of INH. The neurologic conditions were a result of either alcoholism, post-gastrectomy syndrome, nutritional deficiency, or diabetes.

Four of these cases were in on their first admission for treatment of tuberculosis. Clinically, they all did well in regard to both the pulmonary tuberculosis as well as the neurologic symptoms. All were dismissed from the hospital, after six months or more of therapy, three being classified as having inactive tuberculosis and the fourth was discharged with apparently negative sputum but an open healing cavity.

One hospitalized chronic patient receiving INH developed peripheral neuritis which cleared when placed on Salizid therapy. This case was complicated by a nutritional deficiency, so that we could not be entirely certain that the neuritis was completely a result of INH. However, whatever the cause, it cleared during treatment. The sixth case had neurologic symptoms due to a spinal cord compression. The severity of symptoms was reduced during Salizid administration, however, the chronic, minimal tuberculous focus in this patient has been unchanged.

The last case in this group presented a diagnostic chest problem. In addition he had a chronic, progressive neurologic disease, which made INH therapy precarious. However, following one year of Salizid, he was released from the hospital with a negative sputum and no aggravation of the neurologic condition either during or following the period of Salizid therapy.

SM-PAS Failure

A man with a persistent open cavity, positive sputum and laboratory studies indicative of resistance to both streptomycin and PAS was on his initial treatment with INH. Salizid 100 mgm. t.i.d. was added to his SM-PAS therapy. Eleven months later, he was discharged with a diagnosis of inactive tuberculosis.

Seriously Ill Admissions

One of the cases in this group, a first admission, required, because of severity of lesions, what can be considered as heroic treatment. Salizid 800 mgm. a day with pyrazinamide 3 gm. a day was selected. The hospital course thereafter was uneventful. Examination of the lobe resected 11 months later revealed only a 1 cm. epitheloid cavity and no soft caseous nodule. The PZA was stopped after 14 months. He remains on Salizid 800 mgm. a day with no evidence of adverse effects.

One of the cases listed under peripheral neuritis can be included also in this group of desperately ill patients. In addition to having far advanced pulmonary tuberculosis and severe nutritional deficiency, he pre-

sented tuberculous peritonitis and a history of alcoholism and chronic liver disease. There was evidence of abnormal liver function. Running a stormy, febrile course with alternating brief remissions and exacerbations, he received in a three month period, varying combinations of streptomycin, INH, PZA, tetracycline and oxytetracycline; and death seemed imminent. Following these various therapies, and as a last resort, he was placed on Salizid 300 mgm. a day and streptomycin 1 gm. twice a week. The clinical course was uneventful. It is difficult in retrospect to separate the findings of severe disease from those of drug reactions during the first three months, however, the clinical improvement upon shifting to the SM-Salizid in this case was definite.

INH Resistant Cases

Included in this group of INH resistant cases receiving Salizid are the seven cases from the toxicity study, one of the neurologic cases, and an additional case resistant to INH. Large doses up to 1600 mgm. were given. In some instances the clinical impression was that the advance of the tuberculous lesion was slower than it would have been had the patient gone untreated. However, the effect of Salizid in these INH resistant cases was not impressive enough to encourage us to continue Salizid therapy indefinitely. In another instance we employed Salizid, 800 mg., in a patient whose tuberculosis was rapidly increasing in severity. These lesions appeared to be arrested, but we could not attribute the therapeutic benefit obtained entirely to the Salizid, as other chemotherapeutic agents had been administered concomitantly. However, in spite of clinical improvement the cavity has not closed after five months of therapy.

SUMMARY

Salizid, the salicylaldehyde salt of INH, was tried in a series of 18 cases. In a toxicity evaluation doses up to 1600 mg. daily were employed for as long as 10 months. No evidence of neurotoxicity or hepatic damage was obtained from EEG tracings, liver functions tests, or post-mortem examinations. In addition, it is well tolerated in doses of 300 mgm. daily by patients having neurologic disease even with peripheral neuritis resulting from INH. Cases resistant to INH do not respond to larger doses of Salizid. When given in combination with other chemotherapeutic agents, in advanced pulmonary tuberculosis it may be of some benefit. Salizid is an excellent drug and merits further usage in pulmonary tuberculosis because of its safety and chemotherapeutic action in cases of INH sensitive tubercle bacilli.

RESUMEN

El Salizid, que es el salicilaldehido de INH, se ensayó en un grupo de 18 casos. Al valuar su toxicidad se usaron dosis hasta de 1.600 mgr. diarios hasta por diez meses. No se encontró evidencia de neurotoxicidad o de daño hepático según los ECG, las pruebas de función hepática o los exámenes postmortem. Además, es bien tolerado a la dosis de 300 mgr. diarios por enfermos con afecciones neurológicas y aún con neuritis periférica consecutiva a la INH.

Los casos resistentes a la INH no responden a dosis más grandes de

Salizid. Cuando se da combinado con otros agentes quimioterápicos en tuberculosis pulmonar avanzada, puede ser de alguna utilidad.

El Salizid es una droga excelente y merece que se le use más en tuberculosis pulmonar por su seguridad y su acción quimioterápica en casos de bacilo tuberculoso sensible a la INH.

RESUME

Le "salizide," sel salicylaldehyde de l'isoniazide, a été essayé sur un groupe de 18 malades. Pour évaluer la toxicité de ce produit, des doses allant jusqu'à 1600 mmgr. par jour furent utilisées pendant une durée atteignant dix mois. On n'obtint aucune preuve de neurotoxicité ou d'atteinte hépatique d'après les tracés encéphalographiques, les tests de la fonction hépatique, et les examens post-mortem. De plus, il fut bien toléré aux doses de 300 mmgr. par jour chez des malades ayant des affections neurologiques, avec atteinte périphérique résultant de l'isoniazide. Les cas résistants à l'isoniazide ne sont pas influencés par des doses plus importantes de "salizide." Lorsque ce produit est donné en association avec d'autres agents chimiothérapiques, dans les cas de tuberculose grave, il peut avoir quelque action favorable. Le salizide est une excellente médication et mérite un emploi plus étendu en tuberculose pulmonaire, à cause de son innocuité et de son action chimiothérapique dans les cas de bacilles tuberculeux sensibles à l'isoniazide.

ZUSAMMENFASSUNG

Salizid, das Salicylaldehyd-Salz von INH, wurde erprobt in einer Reihe von 18 Fällen. Zur Auswertung der Toxicität wurden Dosen bis 1600 mg. täglich angewandt für eine Zeit von 10 Monaten. Es ergab sich kein Anhalt für Neurotoxicität oder Leberschädigung, wie aus den EEG-Aufzeichnungen, Leberfunktionsprüfungen oder Sektionsbefunden hervorgeht. Ausserdem wird es gut vertragen in Mengen von 300 mg. täglich auch von Kranken mit neurologischen Erkrankungen, sogar mit peripherer Neuritis infolge INH. Gegen INH resistente Fälle reagieren nicht auf grössere Dosen von Salizid. Wird es bei fortgeschrittener Lungentuberkulose in Kombination mit anderen chemotherape-utischen Stoffen gegeben, so kann es von einigem Nutzen sein. Salizid ist ein ausgezeichnetes Mittel und verdient weitere Verwendung bei Lungentuberkulose wegen seiner Harmlosigkeit und chemotherapeutischen Wirkung in Fällen von INH-sensibilen Tuberkelbazillen.

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Bilateral Middle Lobe Syndrome

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Since its first use by Graham, Burford and Mayer,[1] the "middle lobe syndrome" has become well accepted both as a clinical syndrome and as a concept of pathogenesis. Any inflammatory process of the right lung may cause enlargement of the collar of lymph nodes around the long slender middle lobe bronchus with obstruction and distal pneumonitis. This increases the lymphoid tissue response and the obstruction persists with the formation of a vicious cycle, often broken only by surgery, though acute reversible forms may occur.[2] It is also well accepted that an analogous process may involve lobes or segments other than the right middle lobe.

Packard,[3] in 1928, first reported that tuberculous lymph nodes may cause sufficient extrinsic pressure to produce complete bronchial obstruction and massive collapse of the lung even in adults. In 1946, Zdansky[4] and Brock[5] independently pointed out the significance of right middle lobe atelectasis. Zdansky noted that, in children, total lobar atelectasis will frequently be caused by lymph node compression of the bronchi without predilection for any one lobe or bronchus as all bronchi are quite small. In adults, however, atelectasis of an entire lobe occurs with frequency only in the right middle lobe where the bronchus is long, narrow and rendered even more vulnerable by the right angle it forms with the intermediate stem bronchus. In other lobes, segmental bronchial compression with segmental atelectasis is the rule.

Brock, in "The Anatomy of the Bronchial Tree,"[5] also noted the frequency of right middle lobe obstructive pneumonitis. He demonstrated that the right middle lobe bronchus is in the lymphatic drainage pathway of both the right middle and right lower lobes, thereby making it vulnerable from respiratory infections of either lobe. He also mentions the vulnerability of the left upper and lower lobes whose bronchi are surrounded by many nodes at their origin.

As the lingula represents the homolog of the right middle lobe, it has often been referred to as the "left middle lobe." The lingular bronchus is similar to the right middle lobe bronchus in that it is rather long, narrow and bifurcates into two long, narrow divisions. It likewise has a significant cuff of surrounding nodes, but differs in arising from its parent bronchus at a less acute angle which is conducive to better drainage. While the lingula is frequently involved in nontuberculous bronchiectasis, it is less commonly the site of obstructive pneumonitis. In the following two cases, bilateral resections were performed for simultaneous involvement of the right middle lobe and of the lingula with obstructive pneumonitis. This has not been recorded previously.

From the Mississippi State Sanatorium and the Department of Surgery, University of Mississippi School of Medicine.

FIGURE 1 FIGURE 2 FIGURE 3

Figure 1 (Case 1): Roentgenogram of chest showing right middle lobe atelectasis along right cardiac border and slight density in left subhilar area. Most of the retracted lingula is hidden behind the heart.—*Figure 2:* Bronchogram of Case 1 showing bronchiectasis and bronchial clumping of the right middle lobe and lingula.—*Figure 3:* PA roentgenogram of chest of Case 1, three months postoperatively.

Case Reports

Case 1: A 53 year old white woman was admitted to the Mississippi State Sanatorium on March 30, 1955. She had been subject to "bronchitis" since childhood with frequent malaise, colds, fever and a productive cough. She had been seen here for productive cough, weight loss and malaise in September, 1934, at which time x-ray films revealed bilateral apical scarring but no other abnormalities.

In 1945 she started having hemoptyses and increased sputum. Bronchograms in August, 1947, revealed bronchiectasis of the right middle lobe which responded symptomatically to a regimen of postural drainage. In March of 1955 she had an attack of "virus pneumonia" with increased productive cough and hemoptysis. The sputum contained acid-fast bacilli for which she had been placed on streptomycin and PAS prior to admission.

Physical examination showed a well-developed, well-nourished woman (Figure 1). The lungs were clear and the remainder of the physical examination was essentially negative. Sputa on admission were negative and remained so. Other laboratory data were within normal limits. Repeat bronchograms (Figure 2) in July, 1955, revealed extensive bronchiectasis of the right middle lobe and of the lingula of the left upper lobe. Bronchoscopy on July 9, 1955 revealed erythema of the mucosa of the right middle lobe with pus coming from this orifice.

On August 21, 1955 the atelectatic, consolidated lingula was removed. Prominent lymph nodes were noted surrounding the hilum. The postoperative course was completely benign. On November 21, 1955 right middle lobectomy was performed. The lobe was shrunken and consolidated and a prominent collar of calcified nodes was found around the bronchus. The upper and lower lobes were completely free from obvious disease.

Pathologic examination of the lingula showed the specimen to be consolidated with a few small foci of cheesy consistency. Microscopic examination revealed residual nodules of chronic granulomatous inflammation and caseation compatible with tuberculosis. Adjacent tissues showed fibrosis and non-specific chronic inflammation.

Pathologic examination of the right middle lobe revealed marked dilatation of the bronchi, many of which were filled with gelatinous material. Microscopic examination showed bronchiectasis and non-specific chronic pneumonitis but no evidence of tuberculosis.

She was continued on antituberculous treatment and was discharged completely asymptomatic February 23, 1956.

Follow-up one year later showed she was doing extremely well with negative sputa and a clear chest x-ray film.

Case 2: A 49 year old white woman was admitted to the Mississippi State Sanatorium on December 12, 1954. Her past history revealed bronchopneumonia in 1940, and again in 1944, for which she entered a Sanatorium in California where bronchograms and gastric washings were reported as negative. In 1950 she had a severe pulmonary hemorrhage and bronchograms revealed bilateral bronchiectasis. In 1951 and again in 1953 she had "virus pneumonia." On October 30, 1954 she developed chills, fever and productive cough. Sputa were found to be positive for acid-fast bacilli and she was placed on streptomycin and PAS. One week later she developed thrombophlebitis of the left leg which persisted until admission here.

Physical examination revealed a slightly agitated woman with bilateral corneal opacities, enlarged cervical lymph nodes and moderate coarse rales over the right side of the chest. The liver presented two centimeters below the costal margin. The left leg was edematous, dry and scaly with a positive Homan's sign and tenderness along the course of the femoral vein. Sputum cultures were positive from January 18, 1955 until October 18, 1955 but negative thenceforth. Other laboratory data were normal. X-ray films showed infiltrations in the right upper lobe and both lower lung fields (Figures 4 and 5).

Bronchoscopy on September 8, 1955 showed slight erythema of the left main stem bronchus. On October 3, 1955 bronchograms revealed bronchiectasis of the middle lobe, the lingula of the left upper lobe (Figure 6) and the antero-medical segment of the left lower lobe. There was, in addition, minimal cylindrical bronchiectasis of the superior segment of the right lower lobe and the anterior segment of the right upper lobe.

As the sputa remained persistently positive she was placed on isoniazid and pyrazinamide just prior to resection. On October 31, 1955 left thoracotomy revealed nodularity and consolidation of the entire lingular segment with a similar process in the antero-medial basilar segment of the left lower lobe and these segments were excised. On April 9, 1956 right middle lobectomy was performed with no gross evidence of disease being found anywhere else. Thus, in view of her advanced age and limited respiratory reserve it was decided not to remove the superior segment of the right lower lobe or the anterior segment of the right upper lobe.

Pathologic examination of the left lung specimens revealed multiple adhesions, consolidation with small areas of caseation and a 2.5 centimeter cyst of the lingula. Microscopic examination revealed non-specific pneumonitis and bronchiectasis throughout with small areas of granulomatous reaction and caseation. Pathologic examination of the right middle lobe revealed it to be totally atelectatic and consolidated. Microscopic examination revealed marked bronchiectasis with both non-specific and granu-

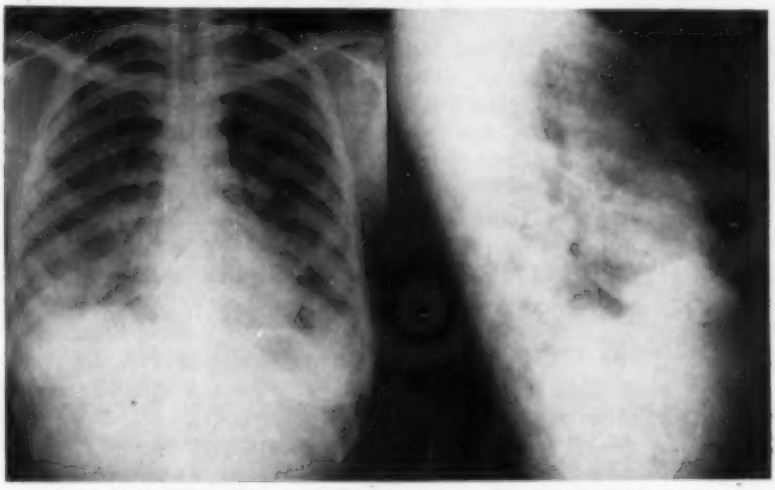

FIGURE 4 FIGURE 5

Figure 4 (Case 2): PA roentgenogram showing infiltrate along right cardiac border and along the left cardiac border in the subhilar area.—*Figure 5:* Right lateral chest roentgenogram of Case 2 showing typical consolidation of the right middle lobe.

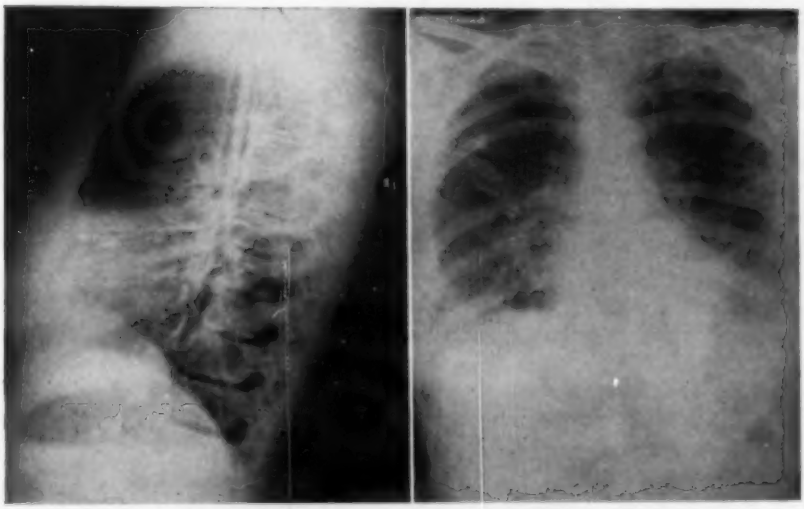

FIGURE 6 FIGURE 7

Figure 6 (Case 2): Left lateral bronchogram showing contracted, bronchiectatic lingula. A similar process can be seen faintly in the anteromedial segment of the left lower lobe.—*Figure 7* (Case 2): Chest x-ray film six months following second operation.

lomatous chronic inflammation. Five months postoperative she had another episode of blood streaking that subsided without clinical or radiologic sequelae. Sputa remained negative and it was thought the hemoptysis had come from residual bronchiectasis in the apex of the right lower lobe or anterior segment of the right upper lobe. She was discharged on November 25, 1956 in good health (Figure 7).

Discussion

Obstructive pneumonitis of a lobe or segment may be caused by an intrinsic lesion such as mucosal edema, fibrosis or plugging (mucoid impaction of Shaw),[6] or by extrinsic compression from lymph nodes or tumor. The right middle lobe is the most susceptible with the lingula being the next most frequently involved. Thus, Paulson and Shaw[7] record 32 cases of right middle lobe syndrome. Of the additional 12 cases of obstructive pneumonitis in their total experience, four involved the lingula. Samson[8] reported 17 cases of right middle lobe syndrome but only seven of right middle lobe bronchiectasis associated with contralateral bronchiectasis which had required resection. The only previously reported case of bilateral middle lobe syndrome found in an extensive perusal of the literature is case four reported by Rubin and Rubin[9] in their 16 cases of right middle lobe syndrome. This was a 29-year-old white man with consolidation and bronchiectasis of the right middle lobe and of the lingula which were demonstrated by x-ray films and bronchograms. No operation was performed in this case. The above cases are the first reported to have bilateral resections for obstructive pneumonitis of the right middle lobe and lingula. Many have been reported, of course, which had bilateral resections for bronchiectasis.

The etiology of nontuberculous bronchiectasis and the middle lobe syndrome are probably similar in that some degree of bronchial obstruction plays a prominent role in each. However, the middle lobe syndrome usually develops in older people and is associated with chronic lobar pneumonitis that is infrequent in the case of bronchiectasis. The middle lobe syndrome apparently persists as chronic pneumonitis because bronchial obstruction is more prolonged or permanent, while in bronchiectasis obstruction is transient or partial. This similarity is emphasized by the second case which had multiple segmental bronchiectasis in addition to obstructive pneumonitis of the right middle lobe, the lingula and one basilar segment.

Rubin and Rubin[9] present evidence that suggests a tuberculous origin of the compression collar of enlarged nodes around the middle lobe bronchus in each of their cases. Cohen[10] likewise stresses the frequency of right middle lobe atelectasis in elderly patients secondary to the reactivation of quiescent tuberculous adenitis which produces gradual compression and frequently perforation of the bronchi. However, many other cases have been found in which tuberculosis was excluded and the nodes were hypertrophied from non-specific inflammation.

Certainly the patients presented here had tuberculosis, the nature of which suggests reactivation in later life in the hilar nodes and not from the usual apical focus. Each had large calcified nodes around the bronchus

on each side. It is interesting that the right middle lobe of the first case showed no granulomatous or caseous pathologic lesions suggesting tuberculosis, although the lingula showed typical tuberculous changes. It is, of course, a frequent finding in resected right middle lobes that the lymph nodes demonstrate tuberculosis and the parenchyma only non-specific chronic inflammatory changes.[11]

Symptomatology is related to bronchial narrowing, leading to recurrent attacks of pneumonia and frequently symptomatic bronchiectasis. There is usually a chronic cough, often spasmodic, occasionally severe, and intermittently productive. Blood streaking or frank hemorrhage is common, due either to the bronchiectasis or to bronchial ulceration by calcified lymph nodes. Persistent wheeze over the affected lobe is suggestive of this diagnosis.

Bronchoscopy may show bronchial narrowing, though often the stenosis is located distally and is demonstrable only by bronchograms or laminograms.

Treatment depends on many factors, such as chronicity of the process, symptomatology, and age and general condition of the patient. Early cases, especially with modern antibiotic therapy, may be completely reversible. In any chronic case, however, only resection is curative. Yet, as many chronic cases are completely asymptomatic and have remained so under observation for many years, the desire for radiologic improvement must be tempered by full evaluation of the patient.

SUMMARY

1. The term "bilateral middle lobe syndrome" has been used to describe concomitant chronic obstructive pneumonitis of the right middle lobe and its homolog, the lingula.

2. Two cases are presented, which are the first reported to have bilateral resections for this condition.

RESUMEN

1. El término "síndrome del lóbulo medio bilateral" se ha usado para describir la neumonitis obstructiva concomitantes del lóbulo medio derecho y de su homólogo que es la língula.

2. Se presentan dos casos que son los primeros relatados que han sufrido resección bilateral para esta afección.

RESUME

1. Le terme "syndrome bilatéral du lobe moyen" a été utilisé pour décrire la pneumonie chronique obstructive simultanée du lobe moyen et de son homologue, la lingula.

2. Les auteurs présentent deux cas, les premiers rapportés pour lesquels cet état a été suivi de résection bilatérale.

ZUSAMMENFASSUNG

1. Der Ausdruck "bilaterales Mittellappensyndrom" wurde benutzt zur Beschreibung der chronischen stenosierenden Pneumonitis, gleich-

zeitig vorkommend im rechten Mittellappen und in seinem Homologon, der Lingula.

2. Bericht über 2 Fälle, die die ersten sind, bei denen aus diesem Grunde eine beiderseitige Resektion vorgenommen wurde.

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Why Do Tuberculous Patients Reactivate?

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A review of the literature reveals uniform acceptance of the fact that a relatively large percentage of tuberculosis patients reactivate regardless of extent of disease,[8, 14, 19] type of treatment whether bedrest,[10] collapse therapy,[9] long[17] or short term chemotherapy or resection.[18] Further, it is accepted that the rate of relapse is usually in proportion to the extent of disease and the amount of physical activity carried on after discharge[12] and is inversely proportionate to the period of hospitalization, with relapse occurring more commonly in men[11] and most relapses occurring within the first three years after discharge. In an article regarding relapse in pulmonary tuberculosis published in 1928, Doctor H. Longstreet Taylor[20] stated that "all apparent relapses are not true relapses, but are evidence of the inherent chronicity of the disease in cases that have apparently improved for a time, but in which the diseased areas have neither healed by resolution nor been encapsulated by the slow process of connective-tissue hyperplasia, and after an uncertain interval, in which no change has been apparent, tubercle has once more begun to spread. . . . Premature discharge of the patient is but an invitation for trouble, since the length of treatment bears an inverse relationship to the percentage of relapses. Relapses are due to attacks of intercurrent disease, serious accidents, childbearing and lactation, to disobedience of the rules in regard to proper methods of work and play, to mental or physical fatigue, to a return to an unhygienic environment, and to many other devious wanderings from the straight and narrow way." . . . I disagree with this attitude which conveniently places responsibility for the relapse on the patient's shoulders and absolves the physician from all blame.

Materials and Methods

On June 1, 1952, we began our present treatment regimen, consisting of streptomycin, para-aminosalicylic acid and isoniazid used concurrently and continuously from admission to discharge, with early resectional surgery when indicated.[1, 2] This is a review of all patients treated between June 1, 1952 and June 1, 1955 who have reactivated as evidenced by positive cultures. There are 330 consecutive admissions with a proved diagnosis of tuberculosis either by positive culture or pathology, including all types of tuberculosis—primary, reinfection, pulmonary and extrapulmonary.[3] Drugs were given in the following dosage: streptomycin gm. 1 twice weekly or ½ gm. for children, para-aminosalicylic acid gm. 10 daily reduced according to weight in children, isoniazid 4 mg. per kilo of body weight daily. Operations were done on 142 patients and 188 were treated only with drugs. All patients received modified bed rest

with full lavatory privileges plus cafeteria as soon as physically able and no collapse therapy either temporary or permanent was done or was rehabilitation training given. All returned to their former occupations upon discharge.[6] The average hospital stay for all patients was 212 days. Six treated medically died of tuberculosis during their hospital stay, while only three died after surgery, one with coronary occlusion, another with pulmonary emboli and one with primary atypical pneumonia. Ten others died of non-tuberculous disease during hospitalization and 14 are known to have died since discharge of non-tuberculous disease.

When drugs were used in courses it was recognized that they were less effective the second time they were given. Reactivation is an obvious indication that the drugs did not sterilize the lesion the first time they were used, therefore it is less likely that they would accomplish this the second try. Because of this, all who reactivated were resected if they were able to tolerate surgery. Those who had serious associated disease have since died so that between resections and autopsies we have pathology from 22 of 24 patients who reactivated. Twenty-three of the 24 returned to our hospital for treatment and the last case (renal tuberculosis) is discussed in detail later.

The radical change in treatment coupled with the fact that all patients have returned to their former occupations regardless of physical activity immediately upon discharge made close follow-up imperative.[6] In our previous experience using three gastric and sputum cultures done in this hospital on patients with x-ray changes characteristic of reinfection type tuberculosis and positive Mantoux, less than 6 per cent of these patients with negative cultures have shown x-ray progression or have had positive cultures within two years of their first admission.[4] Therefore an effort has been made to return as many as possible of these patients, treated since June 1, 1952, for a three day study.

TABLE I
FOLLOW-UP OF DISCHARGED PATIENTS

Number		Reactivations
139	X-ray film plus gastric culture	13
6	X-ray film plus sputum smear and culture	2
92	X-ray film plus clinic visit	8
15	X-ray film sent to us	0
13	Report sent to us	1
32	No follow-up	0
297	TOTAL	24

It is obvious from Table I that we would not have picked up 13 of these patients who were positive on gastric culture only had we depended upon sputum smear and culture and x-ray film change. It has been our experience that a patient may have positive gastric cultures for a year or more before he admits having sputum or before there is roentgenographic evidence of new disease. Only six patients admitted having

sputum and two of them were positive. The balance were seen in clinics by a member of this hospital staff or x-ray films were sent to us for review or reports were sent from other clinics. All but 32 of the entire group (89 per cent) have been followed for an average of more than two years since discharge. If any of these 32 had been hospitalized elsewhere with tuberculosis, our x-ray films would have been requested so we would know about them. We assume some of them are dead and the remainder have not reactivated.

All ex-patients who have x-ray film changes are admitted to the hospital for evaluation. If they have negative cultures and the area clears quickly, they are discharged without further drug therapy. If the cultures are negative and they do not clear thoracotomy is indicated to establish the diagnosis because bronchogenic carcinoma is a good possibility.

The entire group of patients can be divided into those treated medically and surgically (Table II).

When we compare the medically and surgically treated groups there have been no reactivations in minimal disease and none of these patients were resected. When we compare those cases of moderately advanced tuberculosis who received drugs only with those who received drugs plus resection, the surgical group remained in the hospital only 45 days longer, they received about 90 days more of streptomycin and isoniazid and 30 days more PAS, yet the reactivation rate in the surgical group is less than 2 per cent and the reactivation rate in the medically treated group is over 10 per cent. When we compare those cases of far advanced tuberculosis who received drugs only with those who received drugs plus resection, the surgical group remained in the hospital only 14 days longer, they received about 30 days more streptomycin and isoniazid and two days more PAS, yet the reactivation rate in the surgical group is less than 5 per cent and the reactivation rate in the medically treated group is over 12 per cent. Thus those patients who were resected have had fewer reactivations despite the fact that they are hospitalized only a few days longer than the medically treated group and have only a few more days of drug therapy. Of the 17 fusions for bone tuberculosis, none has reactivated even though they have returned to their previous occupations.[7]

The one patient with renal disease who reactivated had one kidney removed some five years before admission here. The ureter from the other kidney is stenosed at the uretero-vesicular junction and has produced a hydronephrosis of the remaining kidney. His blood urea nitrogen and non-protein nitrogen are elevated. The stricture was opened surgically so it was possible to do a retrograde pyelogram by injecting dye rapidly into the bladder, yet the NPN and BUN remain elevated at least twice normal, his urine has contained tubercle bacilli for over a year and these tubercle bacilli are resistant to all commonly used drugs, including streptomycin, isoniazid and viomycin. He now has increasing urinary frequency in spite of continued drug therapy. Certainly obstruction to the outflow path has been a factor in the progression of his disease.

TABLE II

Medical								Surgical						
Number of Patients	Average Hospitalization In Days	Streptomycin	Isoniazid	PAS	Average Follow-Up In Months	Reactivations	Classification of Disease	Number of Patients	Average Hospitalization In Days	Streptomycin	Isoniazid	PAS	Average Follow-Up In Months	Reactivations
16	229	218	205	38	22	0	Primary Tuberculosis							
8	148	162	160	0	11	0	Tuberculous Meningitis							
2	43	182	182	43	12	0	Peritonitis and Adenitis							
4	144	214	214	144	21	1	Renal Tuberculosis	6	156	247	272	159	25	1
							Bone Tuberculosis	17	237	219	189	130	29	0
12	137	196	177	136	25	0	Minimal Pulmonary							
97	175	210	210	135	24	11	Moderately Advanced	55	220	300	293	165	23	1
49	248	277	279	163	23	7	Far Advanced	65	262	310	306	166	21	3

Bronchoscopies using a right angle and fore-oblique telescope have been done on 18 of these patients with pulmonary disease who reactivated. Sixteen had bronchitis as evidenced by increased redness with some edema. Nine had definite stenosis. Stenosis and bronchitis are important factors in reactivation of pulmonary tuberculosis. While bronchitis can be demonstrated in the pathology, bronchial stenosis is seldom reported because the bronchus is commonly cut and sutured at the site of the stenosis.

In analyzing 18 specimens from pulmonary resection and four from autopsy, five basic changes were found: cavity, caseous, tuberculous bronchitis, bronchiectasis and miliary, with two or more often present in the same specimen such as caseous and cavitary disease. Caseation was present in 14, tuberculous bronchitis in 13, cavitary disease in 12, miliary type disease in three and bronchiectasis in two.

The only selectivity between groups treated medically and those treated surgically was first, the 14 retired people who were treated medically because they were not good surgical risks (four of whom reactivated); and second, those who refused surgery during their first period of hospitalization (eight in this group). Five others were not considered for resection for the following reasons: two left against medical advice and their drug treatment was continued for the average time through the health department or private physician; one had essential hypertension but was resected successfully when she reactivated; two had such extensive tuberculosis that we felt resection was too risky during first hospitalization, but both were resected when they reactivated, one died of pulmonary embolus two days post-operatively. The balance of the 23 with pulmonary disease who reactivated (six) had disease which was primarily caseous and after routine anteroposterior tomographs we did not feel that resection was necessary during their first admission; the last patient in this group had renal tuberculosis with one kidney resected previously so the remaining kidney could not be removed.

In culturing resected specimens from patients who had negative gastric cultures before surgery only 11 per cent had positive cultures and another 11 per cent had positive smear and negative culture. Twelve of these resected specimens from reactivations have been cultured and eight (67 per cent) were positive.[5] It is evident therefore that reactivation occurs because of the presence of viable, virulent tubercle bacilli that are not reached by drugs.[15] If reactivation is to be prevented, the types of disease in which these organisms are harbored, namely caseous masses, cavitary disease and serious endobronchial change (bronchial stenosis, bronchiectasis and tuberculous bronchitis), must be resected.

Discussion

A certain percentage of tuberculous patients reactivate regardless of type of treatment and the extent of disease is a definite factor. In this group those with minimal tuberculosis have received drugs only for an average of 196 days and there have been no reactivations at the end of over two years of follow-up. In the cases with moderately to far advanced

pulmonary tuberculosis, those treated with drugs plus resection have had fewer reactivations than those treated with drugs alone. This is true because the type of disease into which drugs cannot penetrate has been removed, namely caseous areas 2 cm. or more in diameter, cavities, bronchial stenosis, tuberculous bronchitis and bronchiectasis. Medlar[16] stresses several things that are of great importance and which have bearing upon what we see in our patients. First, reactivations come from necrotic debris; second, he has never seen a completely healed cavity; third, bronchiectasis peripheral to the stenosis contains debris with viable tubercle bacilli which cannot be completely cleared so that repair can take place.

These patients have not received the long term drug therapy given elsewhere. Such therapy may delay these relapses but will not prevent them as reported by D'Esopo. Because all tuberculous lesions tend to be avascular due to the endarteritis,[13] chemotherapy will be effective before there is extensive destruction, as seen in our minimal cases.

Routine anteroposterior tomographs taken of the entire chest at 1 cm. intervals after three months of chemotherapy will demonstrate most of the lesions which are commonly seen in reactivations and if a lesion that might cause reactivation is suspected then the patient should be bronchoscoped, using right angle and fore-oblique telescopes to find bronchial stenosis.

Most of our patients returned immediately to moderately or heavy work, requiring 2,000 to 3,000 calories per day, yet those doing lightest work—retired people—had the highest reactivation rate, 14 per cent. Our women had the lowest reactivation rate because they came to the hospital for treatment earlier in the course of the disease, they accepted surgery more readily than the men and few left against medical advice. Apparently pregnancy is no factor in reactivation since 18 of our women had 26 pregnancies with no relapse. In all of our reactivations, the ratio of men to women is 3 to 2, but this is almost the same proportion as admissions.

We used only modified bedrest consisting of two rest periods during the day, full lavatory and cafeteria privileges as soon as physically able. No collapse therapy of any kind was done.

A significant percentage of our patients came from the low economic level, many cannot read or write, and for them rehabilitation to lighter work is impossible for they do not have the mental ability to learn. If we order these patients to do no manual labor then they have no alternative but to receive public assistance the rest of their lives. In spite of the fact that we send all patients back to their previous occupations, our reactivation rate is lower than that reported in other institutions where extensive rehabilitation programs are carried on.

The time spent in a hospital is not as important as the treatment that is given during the hospital stay. The purpose of a tuberculosis hospital is to isolate patients while contagious and to treat them so that there is reasonable assurance that they will not reactivate. Since reactivation is

due to the type of pathology present, it is the physician's responsibility to rule out or remove, if possible, these types of pathology. The period of hospitalization for all of these patients was 212 days, this was shortened to 159 days in 1955 and was reduced even further in 1956.

Resistant organisms other than those present on admission have not been a significant factor in reactivation because, using the three drug combination, resistant organisms do not begin to appear until after six months of drug therapy and the 120 original resections were done during the third to fourth month after starting drug therapy. Those patients who reactivated and could not be resected remained positive until death and they developed organisms resistant to all three drugs.

SUMMARY

Reactivation of tuberculosis is due to the presence of virulent viable tubercle bacilli that remain in the tissue. Because of the tendency of the blood vessels in the involved area to be obliterated, chemotherapy does not penetrate into the caseous areas and thick cavitary walls to sterilize these lesions. The other tendency of tuberculosis to obstruct the bronchi with tracheobronchitis prohibits the debris containing tubercle bacilli from being evacuated; therefore this is also a big factor in the reactivation. The extent of disease is a factor because the more extensive the disease, the greater the probability that these serious types of pathology are present. Since the type of pathology present is the main factor in reactivation, our results are as expected. Minimal tuberculosis responds well to drugs only, with no reactivations. In moderately and far advanced disease those patients with resection of these serious types of pathology have fewer reactivations than those who received drugs only. With anteroposterior tomographs and bronchoscopy, using right-angle and fore-oblique telescopes, most of these serious types of pathology can be detected, and it is the physician's responsibility to rule out or remove this pathology before the patient is discharged. Patients have positive gastric cultures for a year or more before they admit having sputum or have x-ray film evidence of new disease, so gastric cultures are necessary to pick up early reactivation. The old ideas that physical exertion, pregnancy, etc., are the causes of reactivation are not true.

RESUMEN

La reactivación de la tuberculosis se debe a la presencia de bacilos virulentos viables que permanecen en los tejidos. A causa de la tendencia de los vasos sanguíneos en el área comprometida, a obliterarse, la quimioterapia no penetra dentro de las áreas caseosas y a través de gruesas paredes caviarias para esterilizar estas lesiones. La otra tendencia de la tuberculosis a obstruir el bronquio por la traqueobronquitis impide que los desechos que contienen bacilos tuberculosos sean evacuados; por tanto, este es también un factor de reactivación. La extensión de la enfermedad es un factor por mientras más extensa es la enfermedad mayor es la probabilidad de que estas graves formas de patología se encuentren.

Puesto que el tipo de lesión patológica que sepresente es el factor mayor de reactivación, nuestros resultados son como se esperan. La tuberculosis mínima responde bien a las drogas solas. En la tuberculosis moderada y muy avanzada los enfermos con resección de estas formas, graves de patología tienen menos reactivaciones que los que sólo reciben drogas. Con las tomografías anteroposteriores y broncoscopías, usando telescopios forblicuos de ángulo recto, la mayoría de estas lesiones serias pueden ser descubiertas y es de la responsabilidad del médico descartar o resecar las lesiones antes de dar de alta a un enfermo. Los enfermos tienen cultivos de lavados gástricos por un año o más, antes de que admitan que tienen esputos positivos y tengan evidencias radiológicas de le enfermedad. Así, es necesario hacer lavados gástricos muy temprano para sorprender pronto las reactivaciones. Las ideas antiguas de que el ejercicio físico, el embarazo, etc., son la causa de la reactivación, no son ciertas.

RESUME

La réactivation de la tuberculose est imputable à la présence de bacilles tuberculeux virulents viables, qui restent dans les tissus. La tendance à l'oblitération des vaisseaux sanguins qui se trouvent dans la région atteinte fait obstacle à la pénétration de la chimiothérapie dans les zones caséeuses et dans les parois cavitaires épaisses. Ainsi ces lésions ne peuvent se stériliser. L'autre tendance du processus tuberculeux qui est l'obstruction bronchique par trachéobronchite empêche l'évacuation des débris contenant des bacilles tuberculeux, ce qui constitue également un facteur important dans la réactivation. L'extension de la maladie est un facteur à prendre en considération parce que plus l'affection est étendue, plus est probable l'existence de lésions graves. Le caractère des lésions étant actuellement le principal facteur de la réactivation, nos résultats sont ceux que nous attendions. La tuberculose minime répond bien aux seuls produits médicamenteux, sans réactivation. Dans la tuberculose à lésions modérées ou très avancées, les malades qui ont subi une résection ont moins de réactivations que ceux qui n'ont été traités que par les médications. La plupart de ces lésions graves peuvent être dépistées par des tomographies antéropostérieures, et des bronchoscopies, en utilisant des optiques à 90° et obliques. Le devoir du médecin est de juguler ou d'enlever ces lésions avant que le malade ne soit autorisé à sortir de l'hôpital. Les cultures de tubages sont positives un an et plus, avant que les malades ne connaissent l'évidence bactériologique ou radiologique d'une nouvelle atteinte, aussi les cultures de tubages sont-elles nécessaires pour dépister précocément une réactivation. Les vieilles idées sont inexactes, selon lesquelles les agents physiques, la grossesse, etc. . . . sont les causes de rechute.

ZUSAMMENFASSUNG

Reaktivierung der Tuberkulose ist die Folge der Anwesenheit von virulenten lebensfähigen Tuberkelbazillen, die im Gewebe bleiben. Wegen der Tendenz der Blutgefässe zur Obliteration in dem befallenem Bereich dringt die Chemotheraphie nicht in die käsigen Bezirke und in die dicken Kavenenwände ein, um diese Herde keimfrei zu machen.

Die andere Neigung der Tuberkulose zur Stenose der Bronchien mit Tracheobronchitis hindert die Tuberkelbazillenhaltigen Zelltrümmer daran, ausgeworfen zu werden; daher ist auch dieser Umstand eine erheblicher Faktor bei der Reaktivierung. Die Ausdehenung der Krankheit ist ein Faktor, denn je ausgedehnter der Prozess, desto grösser die Wahrscheinlichkeit, dass diese ernsthaften Arten von pathologischen Veränderungen vorliegen. Da der jeweils vorliegende Typ von pathologischer Veränderung der Hauptfaktor bei der Reaktivierung ist, sind unsere Ergebisse den Erwartungen entsprechend: die minimale Tuberkulose reagiert gut, wenn nur Medikamente gegeben werden, und ohne Reaktivierung. Bei mässig und bei weit fortgeschrittner Erkrankung zeigen diejenigen Kranken mit Resektion dieser ernsthaften pathologischen Veränderungen weniger Reaktivierungen als solche, die nur Medikamente erhalten hatten. Mit Hilfe von frontalen Schichtaufnahmen und mit der Bronchoskopie unter Verwendung von rechtwinkligen und schrägen Optiken lassen sich die meisten dieser ernsthaften pathologischen Veränderungen auffinden, und der Arzt ist dafür verantwortlich, diese Veränderungen, ehe der Patient entlassen wird, auszuschlissen oder zu beseitigen. Bei Patienten kommen positive Kulturen von Magensäften vor ein Jahr oder länger, ehe sie stationär aufgenommen werden mit positivem Sputum oder röntgenologischen Nachweis einer Neuerkrankung; deshalb ist kulturelle Verarbeitung vom Magensaft nötig, um die Beginnende Reaktivierung herauszufinden. Die bisherige Vorstellung, wonach körperliche Anstrengung, Schwangerschaft usw. die Ursachen der Reaktivierung sein sollen, treffen nicht zu.

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Adrenocortical Pathway of Lobeline Protection in Some Forms of Experimental Lung Edema of the Rat*

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The protective effect of lobeline in pulmonary edema following a.) vagotomy, b.) ammonium chloride intoxication, c.) intravenous adrenaline, d.) intraperitoneal α-naphthylthiourea (ANTU) and e.) chloropicrin inhalation was described in a former paper.[1] These earlier results are summarized (Fig. 1). The mode of action of lobeline remained in this previous work unsettled. It became clear, however, that this protective effect of lobeline is entirely unrelated to its action on the respiratory centers. In this paper some observations concerning the mechanism of this rather surprising action of lobeline are reported. Most of this work was done on CLOP-induced edema of the lungs. This type of edema was preferred because of its well known irresponsiveness to any other drug than lobeline.[1]

Methods and Procedures

Three hundred and nineteen male and female albino rats weighing 150-350 grams were used throughout these experiments.

One hundred and seventy-seven rats were exposed to inhalation of 0.3 cc. 30 lit. CLOP for five minutes. The details of this method are given in our earlier publication.[1] Two animals were simultaneously exposed: the treatment or procedure under trial was applied to one of them while the other served as control.

The first injection of lobeline (Boehringer) consisted of an intraperitoneal dose of 30 mg./Kg. given immediately after the animals were removed from the gas chamber. This dose was followed by the subcutaneous administration of 20, 15, 10, 10 mg./Kg. lobeline every fifth minute.

Twenty-four rats pretreated with 10 mg./Kg. barbiturate (Sevenal), 0.66 cc./100 g. of a 6 per cent soltion of ammonium chloride was given intraperitoneally. Lobeline was given to half of them in a dose of 30-10 mg./Kg. subsequently every fifth minute.

Forty-nine rats were given 20 mg./Kg. ANTU intraperitoneally. (ANTU was dissolved in propylenglycoll). Lobeline was given to half of them immediately after the injection of ANTU in a dose of 20 mg./Kg. Every 15 minutes they received a further 10-15 mg./Kg. dose of lobeline.

Bilateral cervical vagotomy was carried out in 69 rats in ether anesthesia. Within a minute after completing the vagotomy lobeline treatment was started in half of the animals. The first dose consisted of 20

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mg./Kg. subcutaneously, and a dose of 10-15 mg./Kg. was repeated at intervals of 10-20 minutes.

The animals were killed by crushing their cervical spine. Survival time, as calculated from the end of the gassing or from the time of intoxication were about the same in the trial and control groups.

The thorax was opened immediately after death. The heart, oesophagus, thymus and great vessels were carefully dissected off. The trachea was divided at a uniform level. The lungs were weighed to 0.01 g. Lung-body weight ratios were calculated: lung weight was expressed as per cent of body weight. This value will be further referred to as "lung weight."

Lung weight of normal untreated rats was found in this laboratory

The Protective Effect of Lobeline in Different Forms of Experimental Pulmonary Oedema in the Rat

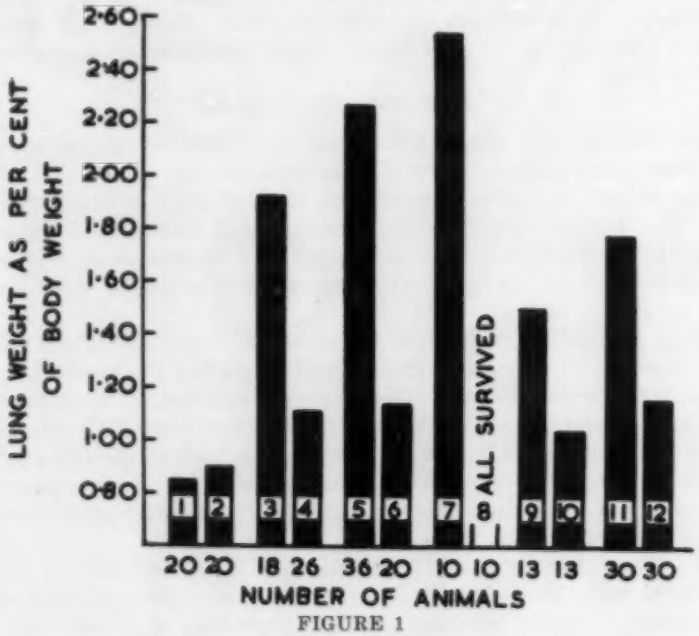

FIGURE 1

1. Normal, untreated controls
2. Normal, lobeline treated controls
3. Vagotomized, untreated
4. Vagotomized, lobeline treated
5. Intoxication with NH_4Cl
6. Intoxication with NH_4Cl, treated with lobeline
7. Intravenous adrenaline
8. Intravenous adrenaline and lobeline treatment
9. Intoxication with ANTU
10. Intoxication with ANTU and lobeline treatment
11. Intoxication with CLOP
12. Intoxication with CLOP and lobeline treatment

0.85 (± 0.07) per cent. Lung weight of intact, lobeline treated rats amounted 0.89 (± 0.06) per cent. In most of the cases measurement of lung weight was supplemented by histologic sections of the lungs. This method of assessing lung edema was found, however, less helpful in our hands.

Statistical evaluation of the results was carried out according to well known formulae.[2]

Adrenalectomy was carried out in 155 of the 319 animals. Bilateral adrenalectomy was done and was followed in most of the cases by a four day period of rest. During these the animals were kept—if not stated otherwise—under a regime of salt water. They all remained in good condition. Others were given desoxycorticosterone acetate (decortone, Ciba), cortisone or hydrocortisone (adresone or hydroadresone, Organon).

In 12 rats experiments were started immediately following the removal of both adrenals. Hypophysectomy was carried out in five. Experiments were started 100 days following this procedure. After killing the animals completeness of hypophysectomy was carefully controlled.

The adrenal medulla was extirpated in seven. Investigations were made 100 days subsequent to medullectomy. A careful post mortem was done in each case which included weighing and microscopic examinations of the adrenal cortex. The weight of the adrenal cortex exceeded in each animal 12 mg./Kg. 100 g. body weight. The finer structure of the cortex was found to be normal.

Results

Results are summarized in Tables I and II and Figures 2 and 3.

Mean lung weight of 26 normal gassed but otherwise untreated animals amounted to 1.29 (Group I of Table I), while that of 11 lobeline treated gassed rats was found 0.90 (Group II of Table I). The difference between these two mean lung weights was statistically significant ($t=3.4975$; $P<0.01$). No microscopic evidence of edema formation could be detected in the lungs of lobeline treated gassed rats.

Mean lung weight of 16 adrenalectomized gassed lobeline treated animals amounted to 1.78 (Group IV of Table I). This value was superior to the mean lung weight of Group III of Table I which consisted of adrenalectomized gassed but otherwise untreated rats.

Mean lung weight of 5 hypophysectomized, CLOP-poisoned lobeline treated rats proved to be only slightly elevated (Group V of Table I).

A 4 per cent solution of formaldehyde was given to four intact rats subcutaneously, three times within 48 hours. On the third day the animals were put into the gas chamber. Their mean lung weight was found to be 1.93, highly elevated (Group VI of Table I).

Corticotrophine (Organon) was injected intravenously to four healthy rats 30 minutes prior to gassing. Lung edema formation occurred in all animals, their mean lung weight was 1.62 (Group VII of Table I).

Corticotrophine Z (Organon) was given subcutaneously to 33 intact rats 24 hours prior to CLOP intoxication. Twenty I.U. was given to 11 rats, 40 I.U. to 17, while the rest received 60 I.U. of the long-acting cortico-

trophine. Pulmonary oedema occurred in all of them (Group VIII, a.b.c., Table I). The mean lung weight of the total Group VIII of Table I did not significantly differ from that of Group I of Table I ($t = 0.7573$; $P = 0.50$).

Noradrenaline (Jenapharm) was given to eight adrenalectomized rats in a dose of 50 micrograms prior to CLOP poisoning. At the end of the gassing procedure a dose of 30 micrograms was given followed by another dose of 20 micrograms five minutes later. The development of unusually

TABLE I

ROLE OF THE ADRENALS IN THE FORMATION OF PULMONARY OEDEMA CONSEQUENT TO CHLOROPICRIN INHALATION AND IN THE MECHANISM OF THE PROTECTIVE EFFECT OF LOBELINE

No.	Group	Treatment: Lobeline	Treatment: Other	Number of Animals	Weight of Animals, g.	Relative Lung Weight	Time of Survival Mins.
I.	normals	—	——	26	258 (±13)	1.29 (±0.07)	20 (± 1)
II.	normals	+	——	11	236 (±16)	0.9 (±0.03)	36 (± 7)
III.	adrenalectomy	—	——	7	152 (±21)	1.64 (±0.14)	19 (± 4)
IV.	adrenalectomy	+	——	16	166 (±16)	1.78 (±0.13)	18 (± 5)
V.	hypophysectomy	+	——	5	167 (±11)	1.05 (±0.02)	20 (± 3)
VI.	normals	—	formaline stress	4	126	1.93	21
VII.	normals	—	ACTH 25 I.U., i.v.	4	150	1.62	26
VIII. a	normals	—	ACTH-Zinc 20 I.U., s.c.	11	286 (±21)	1.27 (±0.16)	22 (± 1)
VIII. b	normals	—	ACTH-Zinc 40 I.U., s.c.	17	242 (±16)	1.31 (±0.17)	20 (± 1)
VIII. c	normals	—	ACTH-Zinc 60 I.U., s.c.	5	190 (16)	1.64 (0.58)	20 (2)
IX.	adrenalectomy	+	noradrenaline	8	226 (±12)	2.10 (±0.32)	9 (± 2)
X.	medullectomy	+	——	7	253 (±20)	0.90 (±0.04)	31 (±18)
XI.	adrenalectomy	+	DOCA, 2 mg./die	17	190 (±13)	1.59 (±0.12)	17 (± 2)
XII.	adrenalectomy	—	Adresone 50-100 mg./die	10	210 (±12)	1.34 (±0.07)	21 (± 1)
XIII.	adrenalectomy	+	Adresone 5-100 mg./die	17	186 (± 9)	0.89 (±0.04)	16 (± 2)
XIV.	adrenalectomy recent	+	——	12	230 (± 5)	1.16 (±0.06)	19 (± 2)

Numbers in parenthesis represent standard deviation of the mean.

severe lung edema was observed in all animals: mean lung weight was 2.10 (Group IX of Table I).

Seven medullectomized rats were poisoned with CLOP and subsequently treated with lobeline. Neither macroscopic nor microscopic edema was observed in any of these animals: their mean lung weight remained normal: 0.90 (Group X of Table I).

Desoxycorticosterone acetate (DOCA) was administered to 17 adrenalectomized rats in a dose of 2 mg. daily for five days. The animals were gassed on the fifth day and lobeline treatment was subsequently started. Mean lung weight was 1.59: significantly elevated (Group XI of Table I).

Cortisone and hydrocortisone were given to 10 adrenalectomized rats in a dose of 50 resp. 100 mg. daily for four days. The animals were gassed on the fourth day, six hours following the last injection of the cortical

Role of the Adrenals in the Protective Effect of Lobeline in Chlorpicrin-Induced Lung Oedema in the Rat

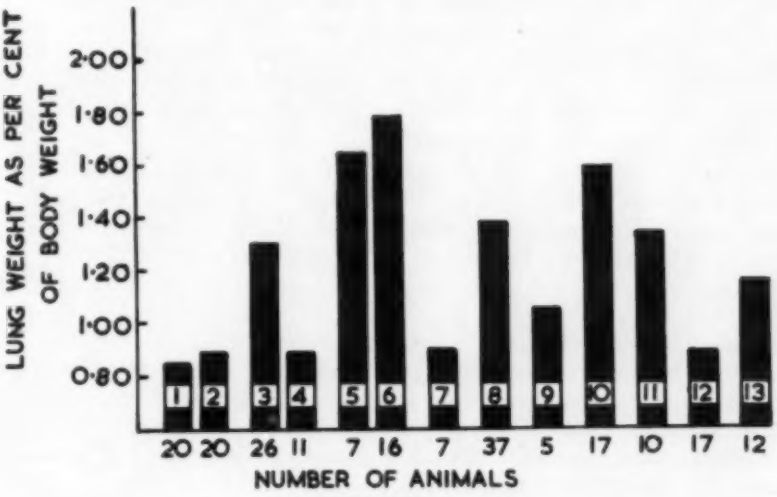

FIGURE 2

1. Normal untreated controls
2. Normals treated with lobeline
3. Normal, untreated, gassed rats
4. Normal, lobeline-treated, gassed rats
5. Adrenalectomized, untreated, gassed rats
6. Adrenalectomized, lobeline-treated, gassed rats
7. Medullectomized, lobeline-treated, gassed rats
8. Normal, ACTH-treated, gassed rats
9. Hypophysectomized, lobeline-treated, gassed rats
10. Adrenalectomized, lobeline-treated, gassed rats, maintained on DOCA (2 mg./day)
11. Adrenalectomized, untreated, gassed rats maintained on cortisone (50-100 mg./day)
12. Adrenalectomized, lobeline-treated, gassed rats maintained on cortisone (2-10 mg./day)
13. "Recent" adrenalectomy followed by gassing and lobeline treatment

extract. Inhalation of CLOP resulted in pulmonary edema: mean lung weight was 1.34 (Group XII of Table I).

Seventeen adrenalectomized rats were given a single injection of cortisone resp. hydrocortisone. The dose amounted to 100, 50, 25, 10, and 5 mg. subcutaneously. Six hours following this injection the animals were exposed to inhalation of CLOP, which was followed by the administration of lobeline. In no case did pulmonary edema appear. Mean lung weight was 0.89 and no histologic evidence of edema formation could be detected (Group XIII of Table I).

Gassing was carried out within 60 minutes following the removal of both adrenals in 12 rats (Group XIV of Table I). Subsequent to gassing lobeline treatment was started. A varying degree of lung edema formation occurred, their mean lung weight did not differ significantly from that of Group II of Table I ($t = 1.1623$; $0.20 < P < 0.30$).

This series of experiments are in a more simple form summarized in Figure 2.

ANTU was given to 24 intact and 25 adrenalectomized rats (Group I of Table II). Lobeline was administered subsequently to 14 intact and 15 adrenalectomized animals. The protective effect of lobeline was not influenced by the removal of both adrenals in this series: the difference between the resulting mean lung weights of the intact and adrenalectomized subgroups was statistically not significant.

Ammonium chloride was given to 12 intact and 12 adrenalectomized rats and all were treated with lobeline subsequently (Group II of Table II). There was no difference in the resulting mean lung weight of the two subgroups: both remained normal (0.95 and 0.89 respectively).

Bilateral cervical vagotomy was carried out in 38 intact and 31 adrenalectomized rats (Group III, Table II). Adrenalectomy itself failed to influence the development of vagotomy-induced lung edema: mean lung weight of the first and second subgroup amounted to 1.37 and 1.38 respectively. Lobeline treatment was, however, by far more effective in the intact subgroup (mean lung weight: 1.03) than in the adrenalectomized rats (mean lung weight 1.25). The difference between these two subgroups was statistically significant ($t = 2.3431$; $0.05 > P > 0.02$).

This series of experiments are in a more simple form summarized in Figure 3.

Discussion

Results of Groups I and II of Table I corroborate our earlier findings (1) concerning the protective effect of lobeline in CLOP edema of the lungs.

Lung weight of adrenalectomized gassed animals (Group III of Table I) exceeded significantly that of normals and remained practically unchanged following lobeline treatment (Group IV of Table I). These observations seemed therefore to permit the conclusion that a.) CLOP edema of the lungs is rendered more severe by the absence of the adrenals, b.) the adrenals play an indispensable role in establishing the protective effect of lobeline.

A slight number of observations reported by various authors speak in

favour of the fact that an increased secretory activity of the adrenal cortices may prevent or ameliorate experimental lung edema. Selye[3] stated that in nephrectomized rats pulmonary edema subsequent to saline infusions could be prevented by the administration of 10 mg. of histamine. In another paper Selye[4] and Halpern, Cruchaud, Vermeil, and Roux[5] pointed out that pretreatment with a minute dose of adrenaline prevented the appearance of lung edema following a large dose of adrenaline. Testoni and Lomeo[7] stated that animals surviving a large dose of adrenaline (the survival was affected by the simultaneous administration of a sympatholytic drug) reach a certain degree of resistance to CLOP edema of the lungs. Koenig and Koenig[6] observed that in their cases formaline-stress inhibited the appearance of pulmonary edema consequent to ammonium chloride intoxication.

We were unable to support any of these observations. Pretreatment with adrenaline did neither prevent nor reduce pulmonary edema due to adrenaine or CLOP (unpublished material). Ammonium chloride edema—according to further unpublished experiments—remained unifluenced in formaline-stressed animals.

Adrenalectomy has an opposite effect in pulmonary edema due to oxygen poisoning:[15] it protects animals against the pulmonary consequences of high oxygen pressure. This however seems to be rather a special characteristic of this type of intoxication.

Recently, some clinical observations were reported concerning the beneficial effect of Prednisolone in more chronic types of lung edema in patients suffering from chronic congestive heart failure.

We were unable to obtain protection by stimulation of the adrenal cortices with formaline stress (Group VI of Table I), or by injecting immense doses of corticotrophine (Groups VII and VIII, Table I) in pulmonary edema following inhalation of CLOP. Serafini and Scapellato[13] have

TABLE II

ROLE OF THE ADRENALS IN THE DEVELOPMENT OF LOBELINE PROTECTION IN SOME FURTHER TYPES OF EXPERIMENTAL LUNG EDEMA

No. of Group	Form of Edema	Adrenals	Lobeline Treatment	No. of Rats	Mean Body Weight, g.	Survival Time, Min.	Lung Weight, Per Cent of Body Weight
I	ANTU	intact	withheld	10	127	190 (± 5)	1.33 (±0.04)
		intact	given	14	162	123 (± 5)	0.97 (±0.04)
		removed	withheld	10	178	187 (± 5)	1.49 (±0.07)
		removed	given	15	183	152 (± 6)	1.06 (±0.04)
II	NH_4CL	intact	given	12	176	33 (± 2)	0.95 (±0.08)
		removed	given	12	250	34 (± 3)	0.89 (±0.04)
III	vagotomy	intact	withheld	21	159	110 (±12)	1.37 (±0.08)
		intact	given	17	163	80 (± 8)	1.03 (±0.04)
		removed	withheld	16	178	114 (±10)	1.38 (±0.09)
		removed	given	15	154	70 (± 6)	1.25 (±0.07)

Numbers in parenthesis mean standard deviation.

either failed to inhibit the occurence of adrenaline lung edema in rabbits by administration of 5-10 I.U. of corticotrophine.

In view of the fact that stimulation of the adrenal cortex even by extreme doses of physiologic and pharmacologic substances remained absolutely ineffective in inhibiting CLOP-edema it seemed unlikely that lobeline protection would be due simply to adrenocortical hyperfunction. This suggestion was further emphasized by our results obtained in hypophysectomized rats (Group V, Table I). In these animals lobeline remained effective. Some other mechanism, rather independent of the anterior pituitary had to be searched for.

Anitchkow[8] and Kuznetzow[9] demonstrated years ago that lobeline increases the secretion of adrenaline. It was attempted therefore to investigate the signficance of the adrenal medulla in the protective effect of lobeline. Nor-adrenaline—as indicated in Group IX of Table I—rather increased lung edema formation in CLOP-poisoned adrenalectomized rats.

The Protective Effect of Lobeline in Various Forms of Experimental Lung Oedema in the Rat as Affected by the Removal of Both Adrenals

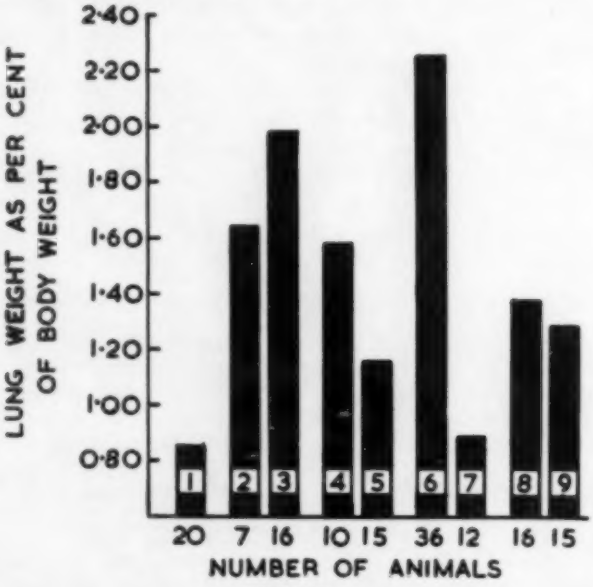

FIGURE 3

1. Normal, untreated controls
2. Adrenalectomized, untreated, gassed rats
3. Adrenalectomized, gassed, lobeline-treated rats
4. Adrenalectomized, ANTU-poisoned, untreated rats
5. Adrenalectomized, ANTU-poisoned, lobeline-treated rats
6. Normal, NH_4Cl-poisoned, untreated rats
7. Adrenalectomized, NH_4Cl-poisoned, lobeline-treated rats
8. Adrenalectomized, vagotomized, untreated rats
9. Adrenalectomized, vagotomized, lobeline-treated rats

On the other hand, lobeline was found to be fully effective in medullectomized animals (Group X of Table I). These observations seemed to indicate the conclusion that the adrenal medulla has no part in the mechanism of lobeline action.

In the next three groups of experiments the effect of adrenal cortical steroids was investigated. All these were carried out in adrenalectomized animals.

Extreme amounts of cortisone and hydrocortisone failed to influence lung edema formation (Group XII of Table I). DOCA given to adrenalectomized animals was ineffective in reestablishing lobeline protection (Group XI of Table I). On the other hand if lobeline was administered to adrenalectomized, cortisone treated rats (Group XIII of Table I), inhalation of CLOP failed to result in lung edema: mean lung weight in these rats was identical to that of intact, lobeline-treated, gassed animals (Group II of Table I). The protection was equally complete whatever the dose of cortisone has been between 5-100 mg. The effect of smaller doses of cortisone was not investigated. The effect of cortisone preadministration depended only from the time of the injection: it had to be given not more than six hours before the experiments.

From these experiments it was concluded that both lobeline and cortisone if given separately to adrenalectomized rats are ineffective in preventing pulmonary edema. These data support the concept that though an intact adrenal cortex is essential for the appearance of lobeline protection, cortisone has a supporting role and not an obligatory action.[14] A somewhat similar observation was recently reported by Kelmen[12] who stated that the presence of cortisone permitted to maintain the permeability inhibiting action of salicylates on the hind-paw edema of adrenalectomized rats. In his experiments however larger doses of cortisone were necessary.

Rat adrenal cortices secrete mostly aldosterone and corticosterone:[11] cortisone is secreted only in small amounts.[10] It remains still to be settled which of these three substances is responsible for the permissive action described above.

Mean lung weight of rats in which CLOP-inhalation was carried out immediately subsequent to adrenalectomy (Group XIV of Table I) was inferior to group IV and equal to Group I of Table I. This seems to support the concept that the amount of prefabricated cortical hormones is insufficient to permit lobeline protection.

Does the same mechanism of lobeline action apply to other types of lung edema? The answer to this question was found disturbing.

It is generally accepted that the mechanism of ANTU-edema is much similar to that of CLOP-edema of the lungs. We therefore turned our first attention to ANTU. (Group I of Table II). ANTU edema was found somewhat more severe in adrenalectomized rats. (The difference was however statistically not significant). Adrenalectomy, to our surprise, failed to inhibit the protective effect of lobeline: the extent of lobeline protection was similar both in intact and in adrenalectomized animals. A similar re-

sult was obtained in ammonium chloride intoxication where lobeline remained fully effective in adrenalectomized rats (Group II of Table II), and in aderenaline-edema (unpublished): the protection afforded by lobeline in adrenaline lung edema was unchanged in the absence of the adrenals. In these two latter groups however one could always argue that these large doses of lobeline have a ganglionic blocking effect. Ganglionic blockers are well known to inhibit ammonium chloride and adrenaline edema. Logically it was therefore expected that the same will happen in vagotomy-induced lung edema. The contrary has however occurred (Group III of Table II). Removal of both adrenals failed to influence edema formation in vagotomized animals. Despite expectation, no lobeline protection was observed in adrenalectomized animals.

Does the difference in the mechanism of lobeline protection justify a conclusion on the genesis of different types of lung edemas? This and many other points of this work can not be answered at present.

SUMMARY

Large doses of lobeline inhibit lung edema formation in chloropicrin (CLOP) poisoned rats. No protection was observed if lobeline was given to adrenalectomized animals. Hypophysectomy, adrenal medullectomy did not interfere with the protective effect of lobeline.

Stimulation of the adrenal cortex of intact rats by formaline stress or by the administration of adrenocorticotropic hormones, administration of desoxycorticosterone acetate or cortisone to adrenalectomized rats failed to influence lung edema formation even if given in extremely large doses.

Lobeline was fully effective in preventing pulmonary edema in adrenalectomized rats if the animals were given a pretreatment of cortisone. This observation supports the concept that though an intact adrenal cortex is essential for the appearance of lobeline protection, cortisone has a supporting role and not an obligatory regulatory action.

The presence of the adrenals were not necessary to permit lobeline protection in α-naphthyl-thiourea (ANTU), ammonium chloride, and adrenaline induced lung edema.

Lung edema in rats subjected to bilateral cervical vagotomy did not respond to lobeline in the absence of the adrenals.

Our thanks are due to Messrs. Organon Ltd. (Oss, The Netherlands) for a generous supply of hormone preparations. Invaluable suggestions and help given by Dr. E. Kelemen is gratefully acknowledged. Funds for this work were made available by the Army Medical Research Institute through the interest of Col. Dr. I. Kenez.

RESUMEN

En las ratas intoxicadas con cloropicrina (CLOP) la formación del edema se inhibe mediante grandes dosis de lobelina. Si la lobelina se dió en animales adrenalectomizados no se observó que la lobelina protegiese. La hipofisectomía, la medulectomía adrenal no interfirieron el efecto protector de la lobelina.

La estimulación de la corteza suprarrenal en ratas intactas, por medio de stress producido por la formalina o por la administración de hormonas

adrenocorticitrópicas, administración de desoxicorticosterona (acetato) o cortisona a las ratas adrenalectomizadas no influyóen la formación del edema aún dadas a dosis extremadamente altas.

La lobelina fué completamente efectiva para prevenir el edema pulmonar en las ratas adrenalectomizadas si a los animales se les dió un tratamiento previo con cortisona. Esta observación apoya el concepto de que aunque un cortez intacto es esencial para que haya protección con la lobelina, la cortisona tiene un papel de soporte en el edema pulmonar producido por L-naftil-tiourea (ANTU), el cloruro de amonio, y por la adrenalina.

El edema pulmonar en ratas sujetas a vagotomía cervical bilateral no respondió a la lobelina en ausencia de suprarrenales.

RESUME

De fortes doses de lobéline empêchent la formation d'oedème pulmonaire chez les rats empoisonnés par le chloropicrine (CLOP). On n'observa aucune protection si la lobéline est donnée à des animaux après surrénalectomie. L'hypophysectomie et l'ablation médullo-surrénalienne n'empêchent pas l'effet protecteur de la lobéline.

En l'absence de lobéline, la stimulation du cortex surrénal chez les rats indemnes, par des injections de "formaline" ou par l'administration d'hormones adrénocorticotropes, aussi bien que l'administration de grandes doses de cortisone (desoxycorticosterone) chez les rats ayant été surrénalectomisés ne purent empêcher le développement d'oedème pulmonaire.

La lobéline est capable d'empêcher l'oedème pulmonaire chez les rats surrénalectomisés traités par la cortisone.

Un travail ultérieur est nécessaire pour préciser le mécanisme exact de l'effet protecteur de la lobéline dans l'oedème pulmonaire.

ZUSAMMENFASSUNG

Hohe Dosen von Lobel in hemmen das Auftreten von Chlorpicrin-Lungenoedem bei Ratten. Diese Schutzwirkung wird durch Adrenalektomie aufgehoben, blieb jedoch durch Hypophysektomie unbeeinflusst.

Reizung der Nebennierenfunktion durch Formalin-Stress oder durch hohe Dosen des adrenocorticotropen Hormons, Verabreichung hoher Dosen von Cortison oder Desoxycorticosteron hatte die Entwicklung des Chlorpicrin-Lungenoedems nicht beeinflusst.

Die Lobelin-Schutzwirkung bei adrenalektomisierten Tieren wurde durch Cortison-Vorbehandlung wiederhergestellt. Es scheint als ob die Nebennierenrinde über eine unentbehrliche, jedoch keine regulative Rolle verfügte.

Eine ungestörte Lobelin-Schutzwirkung war auch nach Entfernung der Nebennieren bei α-Naphthyl-thioharnstoff-Oedem, bei Ammonium chlorid Oedem und bei Adrenalin-Oedem beobachtet. Entfernung der Nebennieren verhinderte jedoch die Lobelin-Schutzwirkung bi Vagotomie-Lungenoedem.

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SECTION ON CARDIOVASCULAR DISEASES

Ebstein's Malformation of the Tricuspid Valve

Study of a Case Together with Suggestion of a New Form of Surgical Therapy

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Ebstein's malformation of the tricuspid valve was first described by Wilhelm Ebstein in his publication of 1866.[1] The salient features of this defect which are relatively constant are: (1) A dilated right atrium usually to a severe degree, (2) Downward displacement of the tricuspid valve into the right ventricular portion of the heart, (3) Severe distortion of the posterior and septal leaflets of the tricuspid valve by this downward displacement of their attachments. There may or may not be variable associated defects such as a patent foramen ovale or atrial septal defect, fenestrations of the deformed tricuspid leaflets, diminution in the right ventricular capacity, evidence of tricuspid insufficiency, and conduction defects consisting of right bundle branch block with prolonged PR interval.

This association of congenital defects has been recognized rather infrequently since Ebstein's description so that in 1937 Yates and Shapiro, reviewing the literature, added the 16th reported case.[2] Kilby and co-workers[3] recently re-reviewed the literature and added five more cases along with one patient surviving closure of the atrial communication.

It is of interest in the light of the frequent association of conduction defects with this malformation that detailed studies by Yates and Shapiro of the right and left bundles of His revealed no abnormalities of the left bundle branch, and although the course of the right bundle branch was somewhat abnormal it conformed in a general way to that of the normal heart.

Thus far medical treatment has consisted of non-specific management of complications as they appear. These have been decompensation (frequently associated with the onset of cyanosis) and arrhythmias. A significant number of these patients die suddenly presumably of ventricular

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fibrillation. The surgical approach to this congenital malformation has been limited to attempts at closure of the patent foramen ovale or atrial septal defect if such is present. The goal of this palliative procedure is to eliminate the right to left shunt with its resultant desaturation, hematocrit increase, and paradoxic emboli. However, it is probable that the right to left shunt represents a compensatory phenomenon in these patients and its eradication may hasten death by provoking or aggravating right heart failure. In 1956 the Mayo Clinic group reported one survivor out of five cases operated upon by closure of the atrial defect, the other four died soon after surgery or during induction of anesthesia.[3]

It is the purpose of this presentation to offer a more definitive surgical procedure based upon the *in vivo* study of the anatomy in a recently observed case.

Report of Case

The patient was a 10 year old girl who had had cyanosis from birth. Examination and catheterization findings in November of 1952 suggested the diagnosis of Ebstein's malformation. In 1954 the patient was started on digitalis as congestive failure was evident for the first time. Also, at that time it was noted that the hematocrit was increasing. By September of 1955 the hematocrit had reached 66 per cent. In November of 1956 she suffered a left cerebrovascular accident which precipitated the decision to seek surgical treatment

On admission to the University of Minnesota Hospitals for the first time in November 1956, she had right hemiparesis and aphasia. She was deeply cyanotic. Her EKG changes were consistent with the diagnosis of Ebstein's disease with right bundle branch

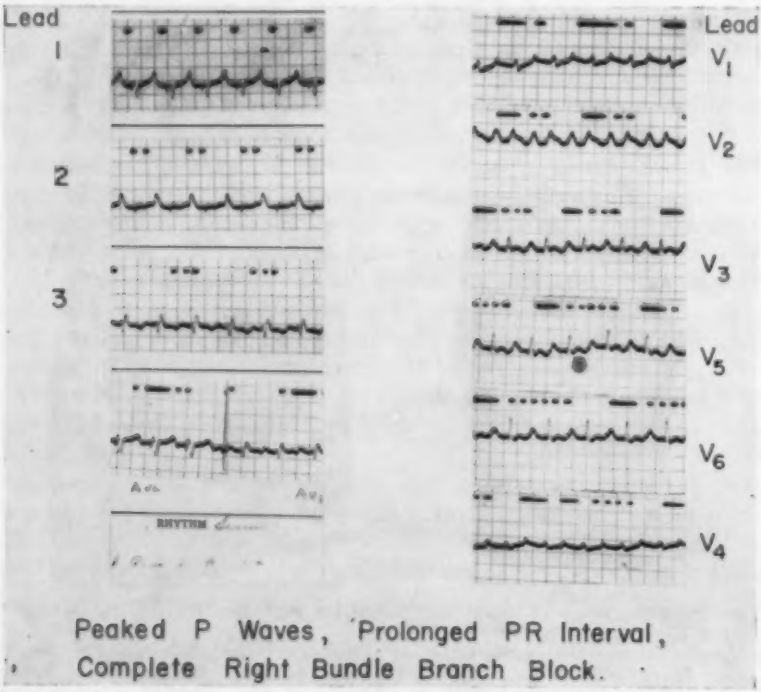

FIGURE 1

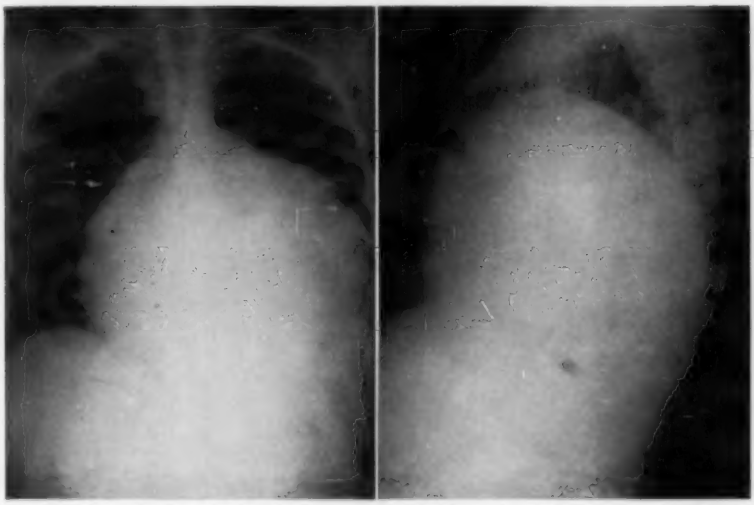

FIGURE 2: Massive cardiomegaly, much enlarged right atrium, large right ventricle, pulmonary artery segment flattened, decreased pulmonary vascularity.

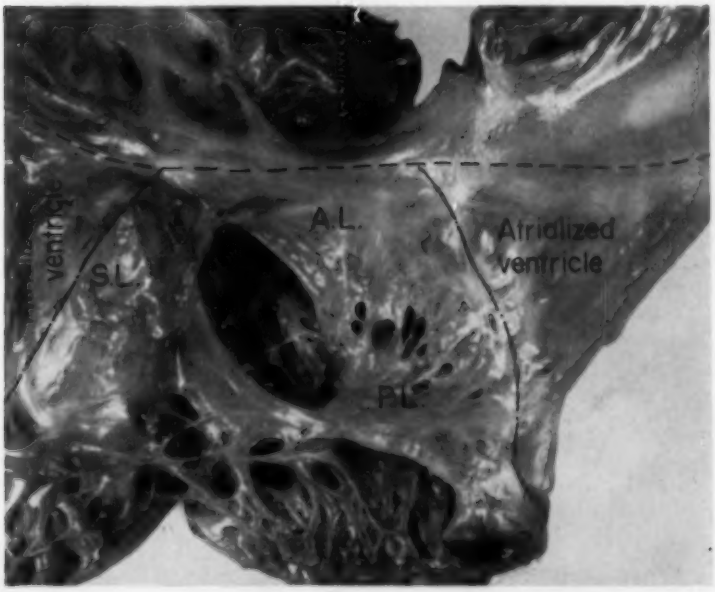

FIGURE 3: View of the displaced Tricuspid valve, note normal position of anterior leaflet, ----denotes true annulus, —.—.—denotes superior border of displaced leaflets. A.L. = anterior leaflet, P.L. = posterior leaflet and S.L. = septal leaflet of Tricuspid valve.

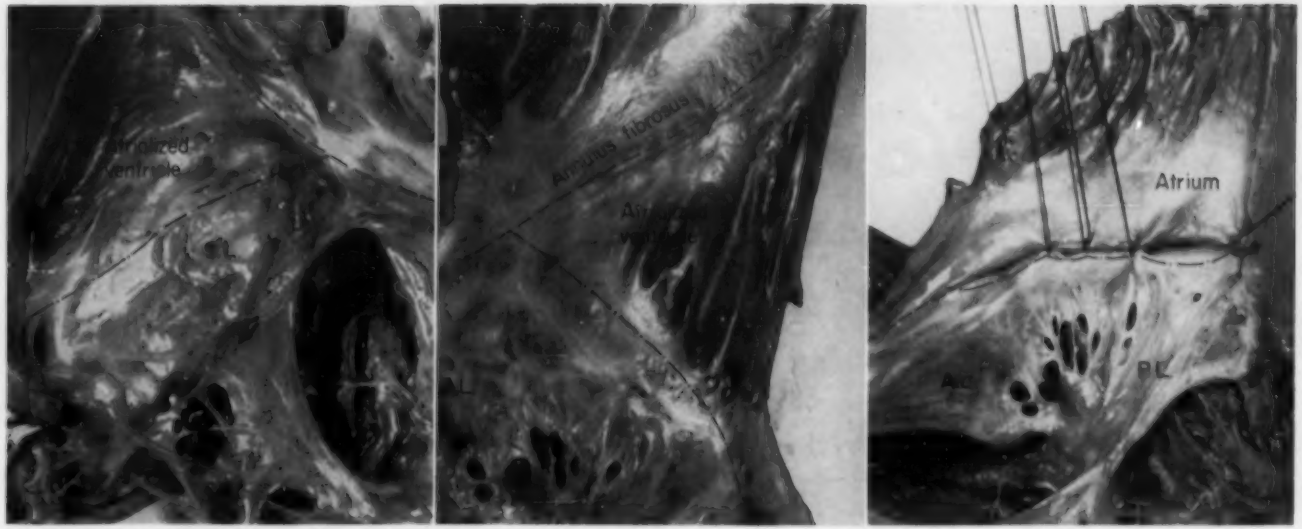

FIGURE 4 FIGURE 5 FIGURE 6

Figure 4: Shows the triangular piece of atrialized ventricle between the septal leaflet and the true annulus which is to be excluded. Distortion of septal leaflet is seen.—*Figure 5:* Shows the triangular piece of atrialized ventricular tissue between the posterior leaflet and the true annulus which is to be excluded from heart. R.A. = right atrium, A.L. = anterior leaflet and P.L. = posterior leaflet of tricuspid valve.—*Figure 6:* The superior border of the displaced posterior leaflet has been approximated to the true annulus fibrosis, The triangular area has been excluded by the plicating stitches.

block, peaked P waves, prolonged PR interval (Figure 1). The roentgen picture was also characteristic (Figure 2). A "box-like" appearance of the heart resulting from the narrowed vascular pedicle and enlarged right atrium were prominent features. A few days after admission, thrombophlebitis of the left leg was noted, and anticoagulant therapy was started. Her condition was considered desperate unless something reparative could be done. It was believed unlikely that simple closure of her patent foramen ovale would provide enough therapeutic benefit to make it worth attempting. The proposed alternative was to utilize total cardio-pulmonary bypass with the pump-oxygenator and under direct vision to attempt a reconstruction of the malformed tricuspid valve leaflets together with closure of the patent foramen or atrial defect. It was thought that this could be done by detaching these malpositioned posterior and septal leaflets and reattaching them more normally. After some slight improvement in her condition, this surgery was planned for December 19, 1956; but she expired during induction of anesthesia.

Examination of the fresh specimen in detail revealed an enormously distended right atrium with a paper-thin wall. The heart, principally the right atrium, contained 3000 cc. of blood. The right atrioventricular annulus measured 19 centimeters in circumference as contrasted to 7 centimeters for the left atrioventricular annulus. The leaflet arrangement of the tricuspid valve was similar to the Ebstein original description (Figure 3). The anterior leaflet was for all intents and purposes quite normal in shape and position though considerably larger than normal. The septal and posterior leaflets were displaced into the right ventricle and were attached far below the normal annular location (Figures 4 and 5). There was no atrial septal defect, but a dilated foramen ovale communication was present.

The Suggested Reparative Procedure

Our previous studies upon this malformation has been based, of necessity, upon the rigid, leathery, formalin fixed specimens available from previous years. These are often completely unsatisfactory for purposes of devising surgical treatment as this case illustrates. In studying possible reparative procedures in this pliable specimen it was noted that the malpositioned leaflets could be repositioned more normally by a simpler maneuver than had been planned.

It was possible, in the fresh specimen, and through a right atrial cardiotomy, to place a row of interrupted silk stitches between the true annulus and the false annulus (i.e. the tissue just above the abnormally placed leaflets) (Figures 3 to 5). When tied, these stitches, having been placed with one bite in the true annulus and the other in the false annulus, pulled the posterior leaflet up to the true annulus by plicating outward a fold of the very thin atrialized ventricular wall (Figure 6). The right coronary artery must be safeguarded in the placement of these stitches. As a result of this plication, the triangular shaped piece of ventricular muscle folded outward would no longer function as an integral part of the right atrium. The identical procedure was carried out for the septal leaflet. This plication maneuver would appear simpler, quicker and more feasible than the previously considered procedure of cutting the leaflets free and reattaching them in a more normal position.

The septal portion of this plication operation would perhaps be somewhat more difficult in that there is not the mobility of the septum comparable to the posterior wall of the right ventricle. Nevertheless, it was possible to oppose the annulus fibrous at the septum with the septal leaflet. Moreover, it is proposed that any large and obvious fenestrations in the leaflets themselves should be repaired with fine silk sutures and the atrial defect, if present, closed. As the displaced leaflets were brought up to

the annulus in this specimen there was also produced a shortening or snugging up effect upon the annulus, which in this case seemed beneficial. If considerable tricuspid incompetency were still present after plication, the diameter of the atrioventricular ring could be further shortened by placement of a few horizontal mattress stitches tied over small Ivalon pledgets, such as has been utilized for the correction of mitral insufficiency.

One is of course disturbed by the paucity of valve tissue present in the small nubbin-like septal leaflet, but it seemed quite likely that the other two leaflets with their more abundant leaflet tissue should be adequate to complete the atrioventricular closure during ventricular systole, particularly since the anterior leaflet in this specimen had undergone compensatory enlargement. In summary, the multiple potential accomplishments of this plication operation proposed for Ebstein's malformation would be neutralization of the contrary acting ventricular tissue in the atrium, the reduction in annular circumference, and repositioning of the malposed tricuspid leaflets so that they could function more effectively.

Discussion

The right side of the Ebstein heart beats inefficiently and often paradoxically and this surgical procedure should correct these abnormalities. That is, as the right atrium of the Ebstein heart contracts in systole, the ventricular portion which has been atrialized, relaxes in diastole, and when the right atrium is in diastole, the atrialized ventricular portion is contracting. Since these two triangular shaped areas of the atrialized ventricle would be excluded by the plication with stitches as described, the Ebstein heart might be freed of this paradox and recover some efficiency on this basis alone.

According to Kilby's[3] recent study, approximately one-third of the recorded deaths from Ebstein's malformation were the result of congestive heart failure. Thus, it seems likely that a majority of these patients have congestive heart failure in the terminal stages of their disease. In many Ebstein patients there is no disagreement over the presence of clinically obvious tricuspid insufficiency. However, in other patients this incompetency is not immediately obvious probably being masked by the greatly enlarged and distensible right atrium allowing considerable regurgitation of blood by serving as a reservoir and thus acting as a buffer for the systemic veins and the liver. Also, there is the decompressing effect of a patent foramen ovale which may postpone clinically obvious right heart failure. The proneness of these patients to fatal arrhythmias is more difficult to explain, but it is clear that this complication plays a consistently more important role than in most other forms of congenital heart disease. Moreover, cardiac catheterization in this malformation has been more hazardous because of this danger of a serious arrhythmia. It is hoped that the proposed surgical procedure by establishment of more effective right heart function with consequent reduction in the atrial overdistention present might lessen their susceptibility to these arrhythmias. Lev et al[4] have contributed additional information upon these arrhythmias

exhaustively studying a case of Wolf-Parkinson-White Syndrome (short PR interval with a prolonged QRS) in an Ebstein heart. These investigators found an anatomic basis for the arrhythmias occurring in their patient. These abnormalities consisted of a right atrioventricular communication outside the usual conduction system, a communication of the right bundle branch and the right side of the septum, and encasement of the right branch in dense fibroelastic tissue. One gains the impression from their study that these extra-conduction pathways consisting of an intermediary muscle bundle with numerous fasiculi to the right atrial appendage and the parietal wall of the right ventricle are the most important elements in the genesis of these conduction irregularities. This may account for the arrhythmias found in the Ebstein heart and also for the unexplained deaths due to this disease. If so, it is possible that the suggested operative technique might alter beneficially this irregular pathway of conduction by deliberately placing the plicating stitches close enough together so as to interrupt these abnormal atrioventricular pathways.

The proposed operation would necessitate total cardiopulmonary bypass with the pump-oxygenator as previously described.[5, 6, 7] Obviously, a trial in patients who have not reached the terminal stages of myocardial decompensation would offer the best test of this hypothesis.

SUMMARY

A case of Ebstein's malformation of the tricuspid valve has been studied. Because of the relative rarity of this defect and the lack of any adequate medical or surgical treatment, a suggested operation is presented for direct attack upon the deformities. Under direct vision by use of total cardiopulmonary bypass the paradoxically contracting atrialized ventricular tissue would be excluded by plication. At the same time, tricuspid valvular function would be improved by the bringing up of the abnormally placed tricuspid leaflets to their true annulus. Also, any patent foramen ovale or atrial septal defect found present would be closed, and fenestrations in the leaflets of the tricuspid valve repaired by fine stitches. The goal of this proposed operation would be the creation of more effective right heart function.

RESUMEN

Se presenta un caso de malformación de Ebstein de la válvula tricúspide. Debido a la falta de tratamiento médico o quirúrgico adecuado, proponemos una operación para la corrección de esta anamalía. La operación tiene por objeto eliminar funcionalmonte el tejido ventricular situado por arriba de las valvas anormalmente desplazadas de tricúspide, mediante la fijación de su borde de inserción al anillo auriculo-ventricular, utilizando un método a cielo abierto y bajo visión directa con ayuda de circulación extracorporea y exclusión cardio-pulmonar circulatoria temporal. Se piensa que la función de la tricúspide mejoraría de esta manera. Simultaneamente una comunicación interauricular o un orificio de Botal persistente, así como posibles fenestraciones en las valvas de la tricúspide, pordían ser reparados ade-

cuadamente. La meta de la operación seria la creación de un corazón derecho funcionalmente más efectivo.

RESUME

Un cas de malformation d'Ebstein de la Valvule tricuspide a été étudié. A cause de la rareté relative de cette lésion et de l'absence de traitement médical ou chirurgical adéquat, nous avons suggéré une technique corrective. La portion "auricularisée" du ventricule, avec contraction paradoxale, serait exclue vers l'extérieur par plicature, sous vision directe á l'aide de l'appareil coeur-poumon. La fonction de la tricuspide étant améliorée du même coup par l'élévation des feuillets valvulaires au niveau de l'anneau trio-ventriculaire. Les anomalies associées telles que "foramen ovale" ou communication interauriculaire seraient suturées et les orifices dans les feuillets tricuspidiens pourraient être réparés en même temps.

Le but de cette intervention est l'amélioration de la fonction ventriculaire droite.

ZUSAMMENFASSUNG

Ein Fall von Epstein's Missbildung der Valvula Tricuspidalis Wurde beschrieben. Die relative Seltenheit dieses Defects erklart den Mangel an adequater chirurgischer oder interner Behandlung. Ein directer operativer Angriff der Missbildungen durch totale Herz-Lungen Ausschaltung unter Sicht ist hiermit empholen. Das sich paradox, Verhof ahnlich contrahierende Kammer Gewebe wird durch Plikation ausgeschlossen. Zur gleichen Zeit kann durch Hebung der Klappen zu ihrem wahren Ring die Funktion der Valvula Tricuspidalis verbassert werden. Ebenfalls kann ein offener Foramen Ovale oder ein Vorhof Septum Defect geschlossen werden und Fenestrierungen der Tricuspidal Klappen mit feinen Nahten repariert werden. Die Verbesserung der Funktion des rechten Herzens ist das Ziel des vorgeschlagenen chirurgischen Eingriffes.

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Convulsive Syncope Due to Rapid Ventricular Arrhythmias

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The clinical manifestations of cerebral anoxia due to failure of left ventricular output are identical, regardless of the cause. Variations in the symptoms and signs of cerebral anoxia are due to differences in duration and intensity of circulatory impairment. Cerebral arteriosclerosis, when present, may exert a profound effect. Thus pallor, faintness, and syncope may occur with asystole of 10 to 15 seconds duration, while with longer attacks cyanosis, convulsions, and stertorous breathing appear. Non-fatal attacks lasting longer than 60 seconds are rare, but do occur.[1]

The names of Morgagni, Adams and Stokes are classically associated with episodes of what Morgagni called "epilepsy with a slow pulse." Gerbezius years earlier had described a patient with intermittent slow pulse, dizziness and slight epileptic attacks. It is interesting to speculate that the carotid sinus may have been hyperactive in Morgagni's patient since he wrote " . . . . . so that we now began to fear, lest the head itself had also contracted the injury, especially as, upon a very quick turn of the head, the epileptic insults recurred, and left a sense of weight with stupidness in the head. . . . ."[2] Many years later vasovagal reflexes were recognized as causes of ventricular diastole producing cerebral anoxia.

More recently[3] identical clinical manifestations have been shown to be due to rapid ventricular arrhythmias which impair left ventricular output. Of 64 cases reported by Parkinson et al.,[4] 13 had ventricular tachycardia or ventricular fibrillation without ventricular standstill, 33 had ventricular standstill alone and 18 had ventricular arrhythmias with periods of ventricular standstill. Between syncopal attacks a majority of those with ventricular arrhythmias had complete heart block, and the others (4 of 31) had partial blocks.

We have recently observed four patients in whom ventricular arrhythmias caused cerebral manifestations. These cases illustrate some of the problems in management of these arrhythmias, especially in the presence of atrio-ventricular block.

Case Reports

Case 1: E. G., a 68 year old white woman was admitted with a history of congestive failure six months previously for which she was digitalized. Her blood pressure was 130/80, and the apical rate was 74/minute and grossly irregular. There was moderate cardiomegaly, but no evidence of failure. The admission electrocardiogram (Figure 1A) showed atrial fibrillation. Maintenance digitalis was continued, and the rhythm converted to sinus with quinidine (Figure 1B). She was maintained on 400 mg. quinidine four times daily at home and did well for 10 days, but then she became angry and fainted. When readmitted, atrial fibrillation was again present and quinidine was increased to 600 mg. four times daily. Tracing two days later (Figure 1C) demonstrated a supraventricular rhythm without conducted P waves at a rate of 50/minute.

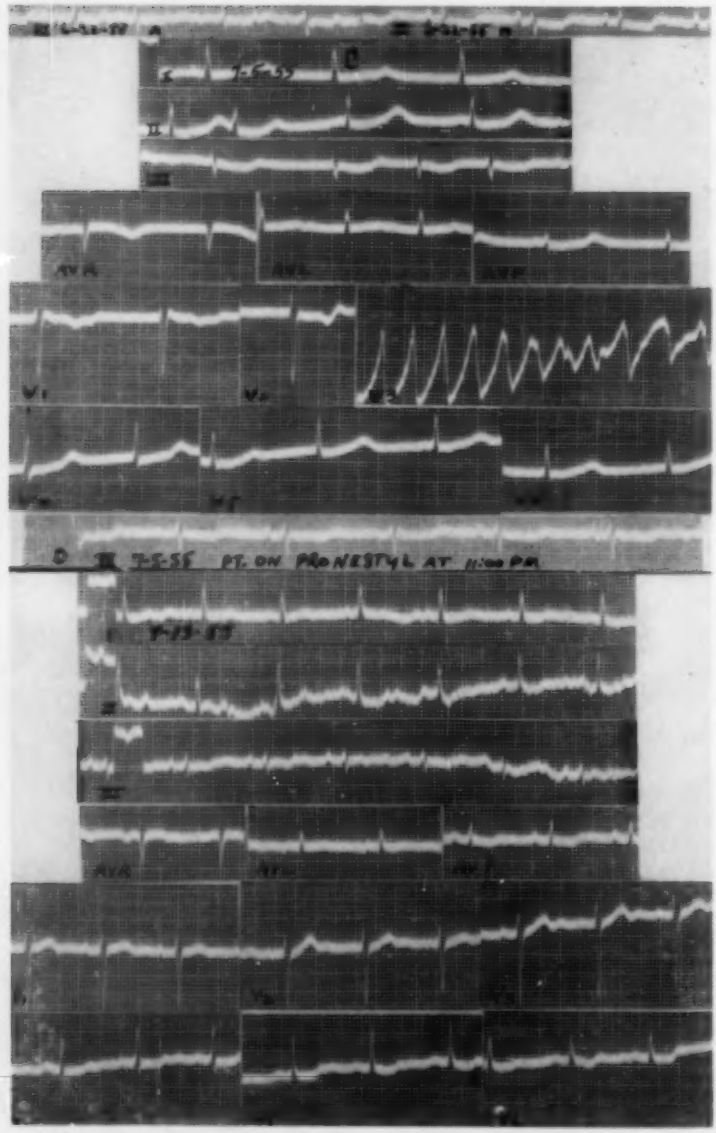

FIGURE 1

FIGURE 2

Figure 1 (Case 1): This series of electrocardiograms demonstrates toxic effects of quinidine including A-V dissociation, prolonged QT interval and ventricular fibrillation which disappeared when procaine amide was substituted.—*Figure 2* (Case 1): Eight days after an episode of ventricular fibrillation there is no evidence of ventricular hyperirritability.

A ventricular complex arose from the descending limb of T in lead II and the QT intervals were very prolonged (0.64 sec.). While V3 was being recorded she had a syncopal attack identical to the one prior to the second admission. The grossly abnormal rhythm was ventricular fibrillation. Examination revealed absence of pulse and heart tones. The episode lasted only a few seconds. Quinidine was discontinued and procaine amide (Pronestyl) 250 mg. four times daily begun. Sinus rhythm had been restored six hours later (Figure 1D).

A follow-up tracing (Figure 2) eight days later showed sinus rhythm with normal QT intervals and no evidence of excessive ventricular irritability on a dosage of Pronestyl 250 mg. every six hours.

Comment: This case illustrates that quinidine can produce episodes of rapid ventricular arrhythmia. It was shown by Schwartz et al.[5] in 1953 that quinidine produced transient ventricular fibrillation in patients who had conduction disturbances. Because quinidine depresses the inherent rhythmicity and irritability of the heart it is particularly dangerous where there is A-V dissociation. Procaine amide is generally thought to have a similar action, but in this case smaller doses appeared to prevent fibrillations without toxic side effects.

Case 2: W. J., a 62 year old white woman with generalized arteriosclerosis and symptoms of cardiac failure for two months was admitted with a history of increasingly frequent syncopal attacks for one week. Her blood pressure was 190/60, and the apical rate was about 60/minute and irregular. Examination revealed moderate cardiomegaly, reduced peripheral pulses, and evidence of mild right ventricular failure. Admission electrocardiogram showed complete heart block with a regular idioventricular rhythm at a rate of 38/minute. She was given isopropyl norepinephrine (Isuprel) 10 mg. sublingually every four hours, theophylline ethylenediamine (Aminophyllin) 0.5 gm. rectally every eight hours, pentaerythrital tetranitrate (Peritrate) 10 mg. orally every four hours, mercaptomerin (Thiomerin) 1 cc. intramuscularly and epinephrine in oil 0.25 cc. intramuscularly every four hours. Syncopal and convulsive attacks with cyanosis became more frequent. After atropine and meperidine (Demerol) in small doses were given, the electrocardiogram (Figure 3) showed high grade partial A-V block with periods of A-V dissociation and multifocal ventricular premature contractions. Twenty-four hours later she was still having syncopal attacks and an electrocardiogram (Figure 4A and B) showed short paroxysms of ventricular tachycardia at frequent intervals. Finally she was given 100 mg. of procaine amide intravenously over a two minute period. During the injection she had another convulsion. The electrocardiogram (Figure 4C and D) showed runs of ventricular fibrillation and flutter. Pronestyl was discontinued and the last electrocardiogram before death (Figure 4E) taken with the patient conscious, showed complete heart block. Convulsive episodes became more frequent and severe and she expired 12 hours later.

Comment: This case demonstrates the danger of procaine amide in the presence of A-V conduction disturbances. It also shows that convulsive syncope can occur on the basis of ventricular tachycardia and fibrillation. In retrospect there were early clues that the convulsive attacks were not due to ventricular standstill. The obvious hyperirritability of the ventricles evidenced by the multifocal ventricular extrasystoles, and its aggravation by epinephrine was a warning of impending ventricular tachycardia or fibrillation. It is now generally agreed that quinidine and procaine amide are both contraindicated in the presence of conduction defects because they are prone under such circumstances to cause episodes of ventricular fibrillation. The prevention of rapid ventricular arrhythmias is difficult, if not indeed often impossible when complicated by conduction defects. Isopropyl norepinephrine was used in this case but the dosage was small. Results may have been better if subcutaneous or intravenous administration had been possible.

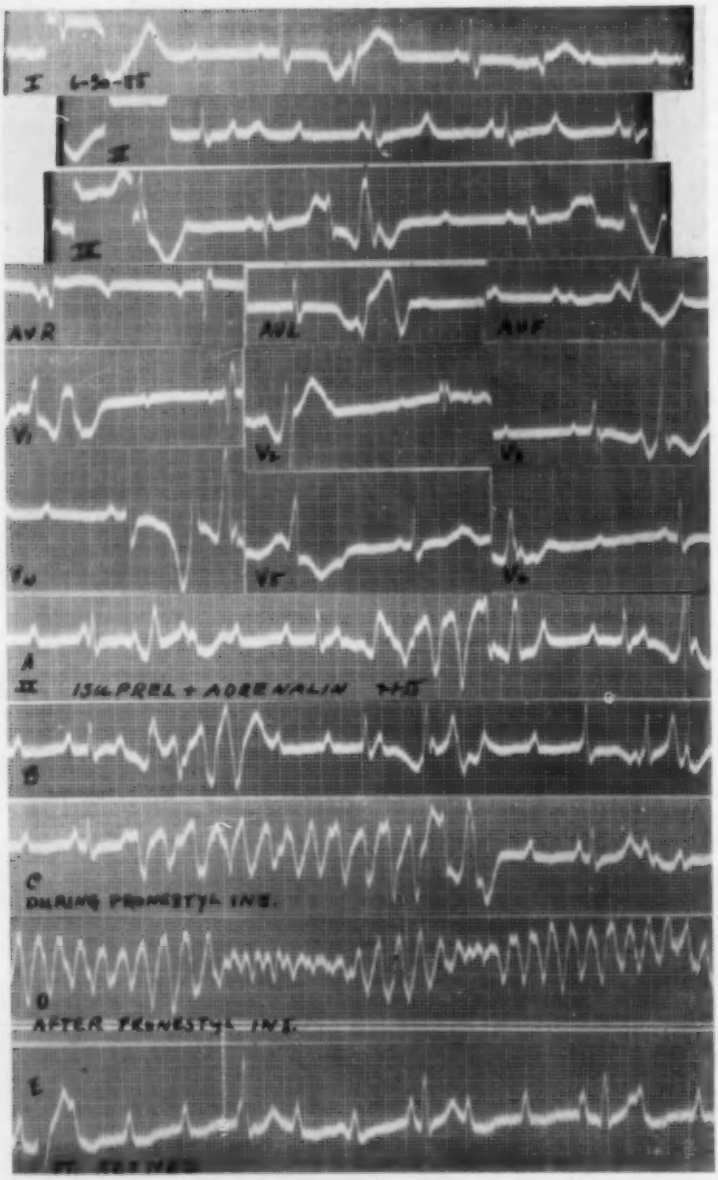

FIGURE 3

FIGURE 4

Figure 3 (Case 2): This figure demonstrates extreme ventricular hyperirritability in the presence of a high grade partial A-V block.—*Figure 4* (Case 2): The ventricular hyperirritability of the preceding figure has now increased to become runs of prefibrillary tachycardia. Pronestyl at this time caused ventricular fibrillation.

Case 3: J. G., an 81 year old white man was seen in the home because of an episode of syncope. His blood pressure was 200/100, the apical rate 48/minute with regular rhythm. He was given ephedrine and pentobarbital sodium (Nembutal), each 25 mg. every six hours. A second syncopal attack occurred two days later, and he was then admitted in acute severe left ventricular failure. The blood pressure was 240/150, and the apical rate about 40/minute but irregular. Following sedation, an electrocardiogram (Figure 5) showed the termination of an episode of ventricular tachycardia which corresponded clinically with syncope and convulsions. He was given 1.6 mg. lanatoside C (Cedelanid) intravenously but died forty-five minutes after admission.

Comment: This elderly male had advanced arteriosclerotic heart disease. The complete heart block was probably on the basis of fibrosis involving the A-V node or bundle above its bifurcation. The idioventricular rhythm was paced by a focus higher than the bifurcation of the His bundle since the QRS complexes are narrow. An acute infarction probably caused the arrhythmia and acute left ventricular failure, but there were no suporting electrocardiographic signs. Intravenous lanatoside C may have increased the irritability of the ventricles and thus contributed to the final episode of ventricular fibrillation. However, the degree of failure made rapid digitalization imperative.

Case 4: C. B., a 75 year old woman was admitted after having several syncopal attacks in the home and ambulance. She was known to have had long standing arteriosclerotic heart disease, and had been digitalized for years. Each observed episode was similar in that she became apneic, cyanotic, and convulsed. During each attack no heart tones could be heard, and no pulse felt. Between attacks she was conscious, and the apical rate was 92/minute and regular. The episodes occurred at intervals of four to five minutes and lasted 15 to 20 seconds. Procaine amide 200 mg. intravenously was given in the home. Upon admission to the hospital fifteen minutes later an electrocardiogram (Figure 6A) was taken. While ventricular fibrillation was being recorded in V3, she had another episode from which she spontaneously recovered. While the electrodes were still in place she became apneic and pulseless, and was given intracardiac epinephrine. The electrocardiogram (Figure 6B) showed ventricular tachycardia at a rate of 180/minute. During this tracing she again recovered for a few minutes more. However, after being given 200 mg. procaine amide intravenously, she expired five minutes later during another attack.

Comment: The sudden onset of symptoms and the variety of rhythms occurring in a subject with known arteriosclerotic heart disease raises the question of myocardial infarction. There was however no pain, and the electrocardiogram is not diagnostic of acute infarction, although there are evidences of old posterior scarring.

The electrocardiogram (Fig. 6*A*) shows A-V dissociation with a faster atrial (110/minute) than ventricular (100/minute) rate in the standard leads. Ventricular prematures are present singly in leads II, III and AVR and in runs in V2. Ventricular fibrillation is seen in V3 and a supraventricular tachycardia at a rate of 150/minute is seen in V4, V5 and V6. In view of the known propensity of procaine amide to cause ventricular arrhythmias in complete heart block[6] the possibility that some of these arrhythmias were due to that drug cannot be denied. The last electrocardiogram taken five minutes before death shows typical ventricular tachycardia at 180/minute. Heart tones and peripheral pulses were present and she was conscious during this time.

Discussion

Ventricular asystole is classically considered due to ventricular standstill, which can be due either to extreme ventricular bradycardia in or-

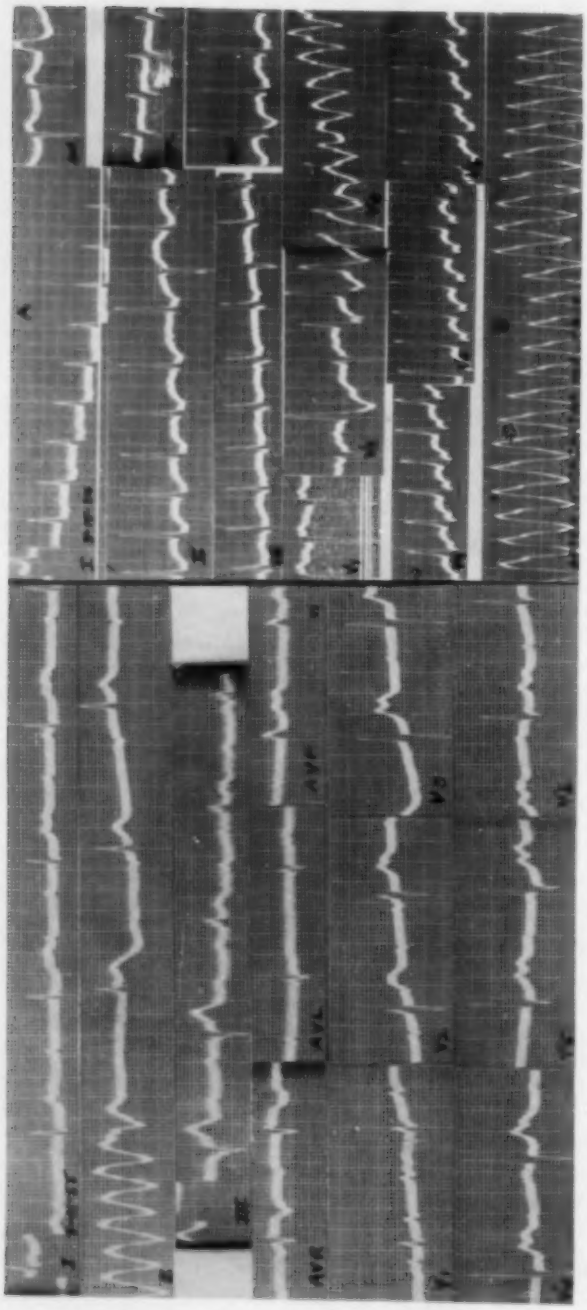

FIGURE 5

FIGURE 6

Figure 5 (Case 3): Complete A-V dissociation in a patient with severe pulmonary edema and syncope with convulsions due to ventricular tachycardia.—*Figure 6* (Case 4): The patient was unconscious and without pulse or heart tones during the tracing of V3. Strip B was made when heart tones and pulse were present, and the patient was conscious.

ganic A-V block or to excess vagal tone in carotid sinus syncope. The block may be due to depression of the conduction mechanism by excess vagus tone or to disease within the conduction system itself, especially fibrosis and anoxia, but sometimes inflammation. Clinically indistinguishable episodes accounting for about one-half of cases of convulsive syncope may however be due to ventricular asystole caused by one of the rapid ventricular arrhythmias. A clinical clue may sometimes be found in palpitation felt by the patient or in recognizing frequent premature beats, but electrocardiographic study is necessary in every case and is the only reliable method by which ventricular standstill and ventricular fibrillation can be distinguished. It is important to make this distinction since logical treatment depends upon accurate diagnosis.[7] It is helpful to think of asystole as being due to a myocardium that is either not irritable enough, as in some cases of A-V block, or too irritable, as in the case of a rapid ventricular arrhythmia.

Rational treatment follows from understanding the mechanism which is causing the attack. Vasovagal syncope is usually effectively treated with atropine or methantheline (Banthine).[8] Surgical denervation of the implicated carotid sinus may be curative, but is rarely necessary.

When the myocardium is not irritable enough and ventricular standstill is causing the attacks, myocardial stimulants are indicated. Epinephrine is classically the drug of choice, usually administered in oil. Because of its ability to cause ventricular arrhythmias it should be used cautiously and only after the syncopal mechanism is known. Barium chloride increases ventricular irritability, but predisposes to ventricular fibrillation and is now rarely used. Ephedrine is similar to epinephrine and can be given orally. All these drugs are contraindicated in cases of rapid ventricular arrhythmias. Standstill and arrhythmias may be found in the same patient at different times. This complicates treatment since the danger of epinephrine producing ventricular fibrillation or perpetuating it is greater than the danger from transient ventricular arrest.

Quinidine and procaine amide are considered drugs of choice in terminating uncomplicated ventricular arrhythmias when heart block, bundle branch block and intraventricular block are absent. In the presence of these frequent complications however, both drugs have the capacity to cause or perpetuate rapid ventricular arrhythmias. If given intravenously, continuous electrocardiographic monitoring is essential.

Schumacher et al.[9] found isopropyl norepinephrine (Isuprel) to be the drug of choice in convulsive syncope. Whereas epinephrine predisposes the heart to ventricular fibrillation, Isuprel stimulates the higher pacemakers without increasing ventricular irritability. By keeping a higher (more rapid) pacemaker active, the ventricular refractory period is prolonged and fibrillation prevented. Isuprel has no effect on junctional tissue, as have quinidine and procaine amide. Having little pressor activity, it is not contraindicated by the presence of hypertension. Isuprel may be administered sublingually in doses of 10 mg. as often as is necessary to prevent attacks. Parenteral dosage forms of the drug are also available.

If used subcutaneously 0.2 mg. as often as every hour may be used. Intravenously, 1 mg. in 200 cc. of 5 per cent glucose may be given at a rate of 10-20 drops per minute as indicated by electrocardiographic monitoring. The value of Isuprel in convulsive syncope complicating heart block is confirmed in a series reported by Wright et al.[10]

Recently[11] a patient with heart block of suspected inflammatory etiology was helped by the use of the anti-inflammatory action of corticotropin (ACTH).

Sodium lactate has been reported[12] of value in cases of ventricular arrest when not due to excess vagal tone. The mode of action is unknown. The possibility of precipitating conjestive failure with large amounts of sodium must be considered.

Electrical stimulation[13] of the heart has proved life saving both in instances of ventricular standstill and in ventricular fibrillation. The value of cardiac massage and electric defibrillation is well known. Supportive measures would include the use of oxygen as arterial oxygen saturation should be raised to as near a normal level as possible. Measures aimed at increasing the coronary blood flow may help to carry the oxygenated blood to the hypoxic conduction system, and thus one or several of the commonly used coronary vasodilators appear worthwhile.

SUMMARY

1. Convulsive syncope due to cerebral anoxia as a result of decreased left ventricular output occurs in ventricular standstill and in rapid ventricular arrhythmias such as tachycardia and fibrillation. Cerebral arteriosclerosis profoundly influences the overall picture.

2. Electrocardiographic study is essential prior to definitive treatment since this is the only certain method by which a distinction can be made between standstill and arrhythmia. Standstill and arrhythmia may occur in the same patient at different times.

3. Myocardial infarction not infrequently causes ventricular arrhythmias.

4. General measures applicable to most patients include oxygen, coronary vasodilators and rest.

5. Uncomplicated ventricular standstill may be treated with epinephrine, but the drug is contraindicated in arrhythmias.

6. Ventricular arrhythmias in the absence of conduction defects may be treated with quinidine or procaine amide. These agents are absolutely contraindicated in the presence of conduction defects because of their tendency to produce ventricular arrhythmias.

7. Isopropyl norepinephrine (Isuprel) is the drug of choice in convulsive syncope. It is not contraindicated in infarctions, hypertension, conduction defects or arrhythmias.

RESUMEN

1. El síncope convulsivo debido a anoxia cerebral acontece como un resultado del rendimiento ventricular izquierdo disminuido en el paro ven-

tricular y en arritmias ventriculares rápidas tales como taquicardia y fibrilación. La arterioesclerosis cerebral influye profundamente en el cuadro general.

2. El estudio electrocardiográfico es esencial antes del tratamiento definitivo puesto que es el único método cierto por que puede distinguirse entre paro y arritmia. El paro y la arritmia pueden ocurrir en el mismo enfermo en tiempos diferentes.

3. El infarto del miocardio no es poco frecuente que cause arritmias ventriculares.

4. Las medidas generales aplicables a la mayoría de los enfermos comprenden: oxígeno, vasodilatadores coronarios y reposo.

5. El paro ventricular no complicado puede tratarse con epinefrina, pero la droga está contraindicada en las arritmias.

6. Las arritmias ventriculares en ausencia de defectos de conducción pueden tratarse con quinidina o amida-procaína. Estos medicamentos están absolutamente contraindicados en presencia de defectos de conducción por su tendencia a producir arritmias ventriculares.

7. En el síncope convulsivo la droga de elección es el isopropil norpinefrina (Isuprel). No está contraindicado en los infartos, en la hipertensión, los defectos de conducción o arritmias.

RESUME

1. Une syncope convulsive due à l'anoxie cérébrale par suite de la diminution du débit ventriculaire gauche peut survenir en cas de pause ventriculaire et dans les arythmies ventriculaires rapides, telles que tachycardie et fibrillation. L'artériosclérose cérébrale joue un rôle important dans le tableau.

2. Une étude électrocardiographique est essentielle avant d'instituer un traitement définitif, puisque c'est le seul moyen certain de pouvoir faire la distinction entre pause ventriculaire et arythmie. La pause et l'arythmie peuvent survenir chez le même malade à des moments différents.

3. Il n'est pas rare que l'infarctus myocardique soit à l'origine d'arythmies ventriculaires.

4. Les mesures générales applicables à la plupart des malades comprennent l'administration d'oxygène, les vasodilatateurs des coronaires, et le repos.

5. Une pause ventriculaire sans complication peut être traitée par l'épinéphrine, mais le produit est contre-indiqué dans l'arythmie.

6. L'arythmie ventriculaire, en l'absence de défauts de conduction, peut être traitée par la quinidine ou l'amide procaïnique. Ces produits sont absolument contre-indiqués en cas de malformations car ils ont tendance alors à être cause d'arythmie ventriculaire.

7. La "norepinephrine isopropyle" (Isuprel) est la médication de choix dans la syncope convulsive. Elle n'est pas contre-indiquée en cas d'infarctus, d'hypertension, de défauts de conduction ou d'arythmies.

ZUSAMMENFASSUNG

1. Kollaps mit Krämpfen infolge cerebraler Anoxie als Folge eines herabgesetzten Schlagvolumens des linken Ventrikels kommt vor bei Herzstillstand, sowie bei rasch folgenden ventrikulären Arrhytmien wie z.B. Tachycardie und Kammerflimmern. Eine cerebrale Arteriosklerose beeinflusst in erheblichem Grade das Gesamtbild.

2. Elekktrocardiographische Untersuchung ist wesentlich vor endgültiger Behandlung, das dies die einzig sichere Methode ist, mit daren Hilfe eine Unterscheidung getroffen werden kann zwischen Stillstand unr Arrhytmie. Stillstand und Arrhytmie können zu verschiedenen Zeiten bei demselben Kranken vorkommen.

3. Myocard-Infarktbildung bedingt nicht selten ventrikuläre Arrytmien.

4. Allgemeine Massnahmen, die bei den meisten Patienten anwendbar sind, umfassen Sauerstoff, coronare Vasodilatatoren und Ruhe.

5. Nicht komplizierter ventrikulärer Herzstillstand lässt sich mit Epinephrin behandeln, jedoch ist dieses Mittel bei Arrhytmien contraindiziert.

6. Ventrikuläre Arrhytmien beim Fehlen von Reizleitungsstörungen können mit Quinidin oder Procain-Amid behandelt werden. Diese Stoffe sind völlig contrindiziert beim Bestehen von Reizleitungs-störungen wegen ihrer Tendenz, ventrikuläre Arrhytmien hervorzurufen.

7. Isopropyl-Norepinephrin (Isuprel) ist das Mittel der Wahl bei Kollaps mit Krämpfen. Es ist nicht contraindiziert bei Infarkten, Bluthochdruck, Reizleitungsstörungen oder Arrhytmien.

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CURRENT THERAPY

The Editorial Board invites your comment.

Treatment of Peripheral Arterial Disease

The purpose of the present report is to review briefly the effective therapeutic procedures and drugs which are being employed currently for the treatment of the peripheral arterial diseases. The treatment of diseases of veins, capillaries and lymphatics will not be discussed. The treatment of the arterial diseases is medical and surgical.

Medical Treatment

Medical treatment consists of 1) protective measures, 2) drugs and 3) physical therapeutic procedures.

Protective Measures:

The patient should: 1) stop smoking, unless he has had a successful sympathectomy, in which case smoking no longer decreases blood flow in the sympathectomized area, 2) walk only to the point of pain, 3) dress warmly, 4) elevate the head of the bed, 5) avoid the foot-up position, 6) not apply heat directly to the feet, 7) not soak the feet in water for long periods unless directed by a physician and 8) use alcohol freely in the form of whiskey if there are no contra-indications.

Drugs:

The agents useful for the treatment of peripheral vascular disease fall into at least the following categories: 1) locally acting agents, 2) systemic antibacterial agents, 3) anticoagulants, 4) muscle depressants, 5) adrenal steroids, 6) vasodilators, 7) vascoconstrictors, 8) positive inotropic agents, 9) vitamins and 10) anticholesteremic agents.

Locally acting agents: These are the fungicides, bacteriostatic, cleansing and proteolytic agents.

Fungicides: Athelete's foot may be kept under control with propionate-caprylate (Sopronol®) powder or ointment, or if this fails potassium permanganate soaks 1:10,000 may be employed.

Bacteriostatic agents: Necrotic tissue should be removed mechanically or by soaks with cleansing or proteolytic agents after which cultures are made to identify the infecting organism. Gram positive organisms often are sensitive to penicillin, 1,000 units aqueous per cc., or to bacitracin in the same dosage. Gram positive mixed with gram negative organisms may be treated with Sulfamylon® 5 per cent and streptomycin 200 units per cc. Pseudomonas aerugonosa and pyocyaneous organisms respond to Aureomycin® ointment 3 per cent or a polymyxin bacitracin mixture (Polycin®) 1 per cent ointment.

Cleansing agents: Aluminum subacetate 0.5 per cent solution in distilled water helps to remove crusts and stop itching.

Proteolytic agents: These remove fibrin and cellular debris. Varidase®

or Tryptar® may be employed. Varidase® is a mixture of streptokinase and streptodornase which are agents excreted by the streptococci. They split fibrin into polypeptides thereby dissolving exudates. Tryptar® is trypsin, a crystilline material from the pancreas which digests non-viable cells but does not attack living cells.

Systemic antibacterial agents: When fever is present cultures from ulcers may suggest the offending organism. Sensitivity tests dictate the type of drug to be used. The gram positive organisms generally respond to penicillin. Gram negative organisms respond to streptomycin. When the organism is unknown a combination of penicillin and streptomycin intramuscularly gives a broad spectrum of antibacterial activity. A wide spectrum of antibacterial action is obtained with oxytetracycline (Terramycin®) orally.

Anticoagulants: These are used for the prophylaxis of arterial thrombosis or embolus, in patients with atrial fibrillation or mural thrombosis, after trauma to vessels from frostbite and after crush injuries. They are contraindicated in patients with abnormalities of the clotting mechanism, liver disease, late pregnancy, advanced renal disease, recent peptic ulcers, subacute bacterial endocarditis, necrotizing arteriolitis, aneurysms of the aorta or when reliable prothrombin and coagulation tests are not available.

Types of drugs: These are heparin which alters the coagulation time and the coumarin and indandione derivatives which alter the prothrombin time.

Heparin: When a rapid onset of action and a short duration is desired heparin is given six times daily intravenously or intramuscularly. When a longer effect is desired it is given deeply subcutaneously every 12 hours using a highly concentrated solution of 200 mg. per cc. Regardless of the method of administration the total dose in 24 hours is based on body weight. For a 100 pound subject 200 mg., 150 pound subject 250 mg. and a 200 pound subject 300 mg. is administered. Coagulation times are taken every 24 hours just before an injection and should be about 2 times normal or about 20 minutes.

Coumarin and indandione derivatives: These agents are employed for intermediate or long term anticoagulant therapy and are listed in Table I. There are some differences between these agents which involve the size of the effective dose, the time of onset of action, the duration of the effect, the time required for the prothrombin time to return to normal after the drug has been stopped, and the effectiveness of vitamin K as an antidote. Acenocoumarin (Sintrom®) has the advantage of a small oral and maintenance dose with rapid onset of action with moderate duration of effect. Diphenadione (Dipaxin®) has a small initial and maintenance dose with a slower onset of action and longer duration than Sintrom®. Warfarin (Coumadin®) has the advantage of an intravenous route of administration which prevents variations in effect due to absorption, with rapid onset of action. The antidote for all of these agents is fresh transfusions, vitamin K_1 (Mephyton®) orally and parenterally.

Vitamin K is not effective against cyclocoumarol (Cumopyran®) or phenandione (Danilone®).

Muscle depressants: These are effective for most night cramps regardless of their etiology. Quinidine sulfate 0.2 gram or quinine 0.6 gram with Benadryl 50.0 mg. before bed are effective.

Adrenal Steroids: Prednisone (Meticorten®) 30.0 mg. daily, Prednisolone (Meticortelone®) 30.0 mg. daily or ACTH, 40.0 mg. daily are employed in the treatment of periarteritis nodosa and disseminated lupus erythematosus. They are only slightly effective against scleroderma. Prednisone and prednisolone have very little tendency to cause sodium retention and potassium excretion. ACTH is generally used to stimulate the adrenal gland after prednisone and prednisolone have been employed for some time.

Vasodilator drugs: These agents for greatest effectiveness should be employed in combination.

Meprobamate (Equanil®), 400 mg. 3 times a day, is employed to prevent central stimulation of the vasomotor center when vasoconstriction is functional.

The DH alkaloids of ergot (Hydergine®), 0.5 mg. 4 times a day sublingually or 0.25 mg. subcutaneously or intramuscularly, depress the vaso-

TABLE I

Drug	Initial Dose Mg.	Maintenance Dose Mg./Day	Time of Onset of Action-Hrs.	Peak Effect Days	Recovery of Prothrombin or Coagulation Time After Stopping Drug—Days	Antidote
Heparin	75 mg. IVI 100 mg. SC	200 SC	¼	1 hr.	3 hrs. after IV 12 hrs. after SC	Protamine Sulfate Transfusion Toluidine blue
Dicoumarol Dicumarol®	1st day 300 2nd day 200	50-100	36	3	5	Vitamin K_1 or K Transfusion
Ethyl biscoumacetate Tromexan®	1500-1800 divided	600-900 divided	18	1	2	Vitamin K_1 or K Transfusion
Warfarin Coumadin®	65 IVI 85 oral	12.5 oral	24 oral 12-24 IVI	2 oral	4	Vitamin K_1 or K Transfusion
Cyclocoumarol Cumopyran®	1st day 100-200 2nd day 75	12.5-50	24	2	5	Vitamin K_1 Transfusion (K not effective)
Phenindione Danilone®	200-300	25-100	18	2	3	Vitamin K_1 Transfusion (K not effective)
Diphenadione Dipaxin®	1st day 20-30 2nd day 10-15	3-5	48	3	7	Vitamin K_1 or K Transfusion
Acenocoumarin Sintrom®	20 oral	8-12	24	1 and ½ to 2	2-3	Vitamin K_1 or K Transfusion

motor center in the hypothalomus and have a slight sedative and adrenolytic effect which is useful for patients with Raynaud's disease when the upper extremities are involved.

Chlorisondamine (Ecolid®), a ganglionic blocker is useful for the diagnosis of causalgia but is not generally employed for prolonged treatment.

Phenoxybenzamine (Dibenzyline®), 10.0 mg. 3 times a day, is a useful adrenolytic agent which blocks the sympathetic nerve endings and produces vasodilatation in patients with arteriosclerosis obliterans or Buerger's disease.

Three pyridine-methanol (Roniacol®) if given in sufficient doses is a useful vasodilator and has a direct action on the blood vessel wall. A minimum of 100 mg. 4 times a day is given. It is more effective when the Timespan tablet is employed in doses up to 900 mg. daily.

Vasoconstrictor Drugs: Cigarette smoking, ergotamine tartrate (Cafergot®) and ephedrine are employed in erythermalgia.

Positive inotropic agents: Norsuprifen (Arliden®) is a positive inotropic agent which increases the force of the cardiac contraction and increases muscle circulation and is employed for intermittent claudication. The dose is 6.0 mg. three times daily.

Vitamins: VitaminB_{12}, 100 mcg. daily parenterally, is employed for diabetic neuritis and if this provides relief of pain, the agent may be tried orally but is less effective by this route.

Anticholesteremic agents: Although the exact relationship of the blood cholesterol to arteriosclerosis is not known, it seems wise to normalize the cholesterol when it is abnormal. The underlying causes such as diabetes, hypothyroidism and nephrosis should be corrected when possible. When the cause of an elevated cholesterol is not known the following may be employed.

Thyroid preparations: Triiodothyronine (Cytomel®) in doses of 25.0 to 50.0 mcg. daily lowers the cholesterol but should not be given in patients with coronary artery disease as angina may be precipitated. Other thyroid preparations are effective also but with Cytomel the cholesterol level stays down better when it is continued for long periods of time than with some other preparations.

Beta sitosterol: (Cytellin®), one or two tablespoonsful 3 times a day, is certainly effective in many patients as it prevents the absorption of cholesterol in the food. This can be shown clearly with appropriate fat tolerance tests.

Safflower oil: (Saff®) also is effective in a significant number of patients. The dose is one ounce twice daily. It is postulated that the high linoleic acid content is responsible for its cholesterol lowering property.

Estrogens: These lower cholesterol, however, undesirable side effects are produced. New estrogens under clinical investigation may be without these side effects.

Physical Therapeutic Procedures:

Indirect body heating: Moderate heat to the trunk increases the circulation to the limbs. If the heat is excessive the blood in the diseased limb will be directed away from the diseased areas to the more healthy areas. Thus, this procedure should be used cautiously.

Oscillating bed: This is useful in some patients with ulceration of the skin when there is a tendency for swelling to occur. By adjusting the bed with the maximum foot-down and minimum foot-up position throughout its cycle, the arterial circulation to the feet is increased with minimal edema because venous dumping occurs periodically. Vasodilators should be used simultaneously with this treatment.

Leg cradles: These are used without heat or with a 25 watt bulb merely to maintain the skin at normal temperature under the cradle. When the lamp is not employed the legs should be wrapped in stockinette to prevent heat loss from evaporation.

Surgical Treatment

Surgical treatment includes sympathectomy, arterial grafts, vein grafts, plastic prostheses, embolectomy, thromboendarterectomy, arterectomy, arterial shunts and amputation.

Sympathectomy: This increases the circulation to the arms and hands and to the distal thirds of the legs and feet. The procedure is used when disease of small vessels is present (diabetes) or when it is impractical to restore the patency of large arteries by graft or other direct methods. The major indication for sympathectomy is the presence of an increased sympathetic vasoconstrictor tone which is suggested by a history of cold feet during the day with warming of the feet at night, or by cold wet feet and constricted veins which become warm and pink after a diagnostic posterior tibial nerve block which can be carried out as an office procedure. The diseases improved by sympathectomy are arteriosclerosis obliterans, Buerger's disease, diabetes, sympathetic dystrophy, Raynaud's disease and acrocyanosis. The selection of patients for sympathectomy is facilitated by plethysmographic tests.

Arterial grafts: Arterial homografts have been successful for repairing weakened or dilated vessels, to restore patency to obstructed arteries and for temporary or permanent shunts to bypass obstructions in an artery. The homograft is indicated for replacing aneurysms of the abdominal aorta, popliteal arteries, and for the repair of chronic obstruction of large arteries such as the aorta, iliac, femoral and popliteal arteries.

Vein grafts: These are generally less satisfactory than arterial grafts because they tend to dilate and calcify.

Plastic prostheses: Vinyon N, Nylon, Dacron and Teflon have all been employed. Generally arterial homografts are somewhat easier to handle than are the plastic prostheses, although the prostheses have the advantage of ready availability.

Embolectomy: This is indicated usually when an embolus has been

present for only a few hours because after this time proximal or distal thrombosis of the artery occurs. As soon as the embolus is recognized heparin is given intravenously every four hours up to the time of surgery at which time protamine sulfate may be given to stop its effects. Embolectomy usually is carried out when the embolus is lodged in the aorta, iliac, femoral or popliteal arteries. After surgery heparin and dicoumarol are given continuously. The heparin is stopped in a few days and the dicoumarol is stopped in a few weeks.

Thromboendarterectomy: This procedure involves the removal of obstructing material from within the artery, and is indicated when large arteries, such as the iliac and femoral arteries, are obstructed for short distances and the distal arteries are patent. This procedure has the advantage that dilatation of the weakened vessel may occur postoperatively.

Arterectomy: The removal of an obstructed arterial segment was advocated by Leriche who thought that surgery removed an irritating focus which produced vasoconstriction. This procedure is not advisable if an arterial homograft can be carried out.

Arterial shunts: These may be temporary or permanent and consist of arterial homografts which pass around the obstruction. These have been used to bypass obstructions in the superficial femoral artery, the bypass extending from the common femoral artery to the popliteal. There is a slight tendency for these grafts to thrombose after months or years.

Amputation: As a last resort amputation may be necessary. Amputation should be carried out at the lowest possible site.

Other methods of treatment: Peripheral nerve crush is not generally successful because of the adrenalin sensitivity which develops with resultant vasoconstriction. Intra-arterial therapy with Priscoline® and other agents is not generally employed because the effect is fleeting.

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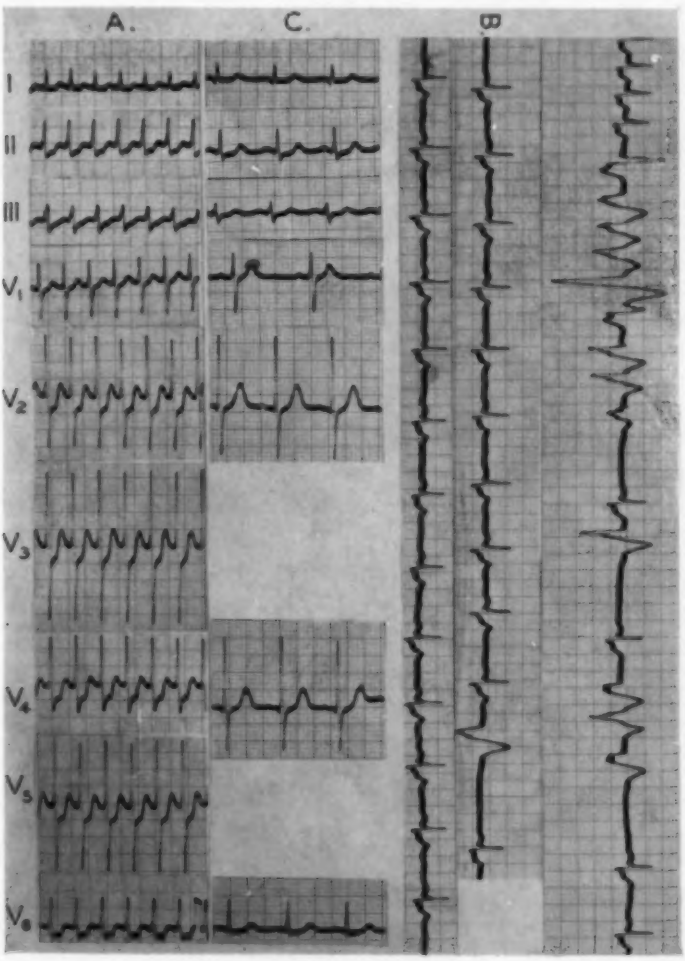
THE ELECTROCARDIOGRAM OF THE MONTH

The authors would be pleased to receive comment and controversy from readers in relation to explanations offered.

A 53 year old woman has had attacks of paroxysmal supraventricular tachycardia about three to four times a year for the past 15 years. She has been known to be hypertensive (220/110) for the same period of time. During the past eight years the tachycardia is soon accompanied by pain in the chest and in the left arm. Recently she appeared in the office with one of these attacks and electrocardiogram *A* was recorded. While lead II was being recorded continuously *(B)* carotid sinus stimulation was applied. Five minutes later record *C* was obtained.

Interpretation: The RS-T shifts observed during the tachycardia *(A)* can hardly be attributed entirely to the very rapid rate. Since they were so pro-



nounced and were accompanied by pain in the chest and the left arm it was decided that they should be followed. Following return to sinus mechanism with very much reduced ventricular rate it is noted that the RS-T shift in part persisted for some time (*B*). After five minutes (*C*) only a very slight shift remains. It was felt that the persistence of the shift demonstrated here implied that a degree of subendocardial "injury" similar to that which occurs in many anginal attacks resulted from the excessive rate. Of course it should be remembered that occasionally an attack of angina will be responsible for supraventricular tachycardia.

Incidentally, when the carotid sinus stimulation induced arrest a short period of ventricular tachycardia occurred (*B*). This alone is of some interest.

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Case Report Section

Congenital Aortic Stenosis, Coarctation of the Aorta and Patent Ductus Arteriosus: Report of Two Cases*

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Aortic stenosis combined with coarctation of the aorta has been reported by a small number of writers. In 1955 Smith and Matthews[1] were able to collect 24 autopsied cases from the literature. Marquis and Logan[2] have listed three additional patients. The clinical diagnosis has been made in a few others.[1, 3, 4] In the majority of instances the aortic stenosis was believed to be an acquired lesion.[1] That the combination is more common than these figures would indicate and that the aortic stenosis may frequently be of congenital origin is attested by its presence in eight of 37 individuals reported by one of us[5] in whom the stenosis could not be considered to be acquired.

Two patients have been seen who, in addition to congenital aortic stenosis and coarctation of the aorta, had a patent ductus arteriosus. Because the ductus introduces certain further physiologic and therapeutic problems, these cases are being reported.

Case Reports

Case 1: E. M., boy age 14. A diagnosis of congenital heart disease had been made at age three months. When he entered elementary school it was noted that on moderate exertion he would tire and become short of breath more quickly than his contemporaries. His activities had always been restricted by the parents. Occasional headaches and frequent epistaxis had been present. There had been no illness suggestive of the rheumatic state.

On physical examination, he was found to be well developed and nourished. There was no cyanosis. Carotid pulsations were visible at rest and the jugular veins were slightly distended. There was a prominent venous pattern over the anterior thorax. The heart was enlarged to the left and downward. A strong systolic thrill was palpable in the second and third right interspaces and over the neck vessels. A feeble systolic thrill was felt posteriorly to the right of the second and third thoracic vertebrae. The cardiac rate was 92/minute and there was a normal sinus rhythm. The sounds were normal. A loud harsh systolic murmur was best heard in the second and third interspaces to the right of the sternum and was transmitted over the entire thorax and to the neck. The right radial pulse was stronger than the left. No pulsation was felt over the arteries of the legs. Blood pressure in the right arm was 112/98; in the left, 102/90. No reading could be obtained in the lower extremities.

On the basis of these findings, diagnoses of aortic stenosis and coarctation of the aorta were made. He was admitted for study.

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Laboratory Data—The electrocardiogram showed left bundle branch block and left ventricular hypertrophy.

On films and fluoroscopy the pulmonary vascular markings were normal. The main pulmonary artery and its right and left branches were normal. In the postero-anterior view the ascending aorta could not be defined. The heart was enlarged 2 plus in mass with rounding of the left border. In the left anterior oblique view the ascending aorta was dilated 2 plus. The data obtained by right heart catheterization are presented in the Table.

Hospital Course—From the catheterization there was evidence of a left to right shunt at the level of the great vessels. This was believed to indicate the presence of a patent ductus arteriosus. The pressure in the right ventricle, pulmonary artery and pulmonary venous capillary bed was elevated. The brachial artery tracing was abnormal, there being a delay to the peak of systole and a notch on the anacrotic limb near the summit. The dicrotic incisura was distinct.

Thoracic aortography was performed to delineate the coarctation believed to be present. The catheter could not be guided into the ascending aorta. Fifteen cc.'s of 70 per cent diodrast were injected in the region of the origin of the left subclavian artery. A short area of coarctation was demonstrated.

He was operated upon by Dr. Charles P. Bailey. When the isthmus of the aorta was dissected free, it was found that the patent ductus measured 0.5 cm. in diameter. It joined the aorta in the area of coarctation. There was a diffuse systolic thrill over the pulmonary artery and ascending aorta. The ductus was divided in the usual fashion. The coarcted segment of the aorta was then resected and an end-to-end anastomosis performed. The thrill over the pulmonary artery could no longer be felt. Through an incision in the myocardium of the left ventricle the aortic dilator was then introduced and the head guided to the region of the valve. The expanding arms were cautiously opened and the stenosed valve dilated. The thrill over the ascending aorta was now definitley less prominent.

Postoperatively the systolic murmur in the second and third interspaces was decreased in intensity and the thrill less marked. There was present a faint early diastolic murmur in the same area. No other sign of aortic insufficiency was found.

Case 2: M. B., girl age 6. A diagnosis of aortic stenosis was made at the age of two years. Her exercise tolerance had always been limited and she would become short of breath on moderate exertion. Profuse perspiration had been noted. Headache was a frequent complaint and she occasionally became dizzy after exertion. Left chest pain had been present on two occasions. The circumstances were not recalled. During the two months prior to admission she frequently said that her legs had "gone to sleep."

On physical examination she was well developed and nourished. The bony thorax was asymmetrical, the left anterior thorax being more prominent than the right. The heart was perhaps slightly enlarged to the left on percussion. There was a systolic thrill in the second and third right interspaces which could be felt over the neck vessels. The cardiac rate was 84/minute and there was a normal sinus rhythm. The second sound at the base to the right of the sternum was faint. A loud harsh systolic murmur was best heard in the second and third right interspaces and was transmitted over the anterior chest and to the neck. A systolic murmur of different character, softer and blowing, was heard over the posterior thorax. Femoral pulsations were weak. Blood pressure was 122/60 in the right arm, 106/80 in the left arm. It could not be determined in the legs.

Laboratory Data—The electrocardiogram showed left ventricular hypertrophy. On films and fluoroscopy the pulmonary vascular markings were accentuated 2 plus. The

TABLE I
CATHETERIZATION DATA

	O_2 Content (Vol. %) (Average of Three Samples)				Arterial Saturation	Pressure (Mm. Hg.)				
	VI	RA	RV	PA		RA	RV	PA	PVC	BA
E. M.	13.2	12.7	12.0	13.1	93 %	(0)	40/0	42/25	(20)	90/60
M. B.	10.4	9.9	9.6	11.3	91 %	(0)	70/0	70/55	(15)	80/60

Key: VI—venous inflow. RA—right atrium. RV—right ventricle.
PA—pulmonary artery. PVC—pulmonary venous capillary.
BA—brachial artery.
Figures in parentheses indicate mean pressure.

main pulmonary artery was dilated 2 plus as was its right branch. The left branch could not be defined. The ascending aorta was dilated and the knob prominent. The heart was enlarged 2 plus to the left with lengthening of the left border. In the left anterior oblique view there was 2 plus posterior prominence of the cardiac shadow. The data obtained by right heart catheterization are presented in the Table.

Hospital Course—From the catheterization there was evidence of a left to right shunt at the level of the great vessels. The pressure in the right ventricle, pulmonary artery and pulmonary venous capillary bed was elevated. The brachial artery tracing showed a slow rise to the peak of systole.

Thoracic aortography was performed to define the extent of aortic coarctation. It was found to be confined to a short segment just distal to the left subclavian artery. There was a suggestion of simultaneous opacification of aorta and pulmonary artery.

The child was operated upon by Dr. Charles P. Bailey. Over the ascending aorta and pulmonary artery a systolic thrill was felt. The ductus was found to be 1 cm. by 1 cm. and to join the aorta in the area of coarctation. It was divided and the narrowed area of the aorta resected. Aortic valve dilatation was then carried out via the transventricular route. No thrill could now be felt over the pulmonary artery and that over the ascending aorta was softer and more diffuse.

The postoperative course was uneventful. The murmur and thrill in the second and third right interspaces were now much less prominent. The posterior systolic murmur could no longer be heard.

Discussion

This complex of anomalies is unusual in that for each malformation a satisfactory surgical procedure exists. The recognition of the presence of all of the components and of their relative severity is necessary.

The murmur and thrill of aortic stenosis were unmistakable in both of these patients. Nothing was heard which would suggest a patent ductus arteriosus. Knowledge of its existence required catheterization. The character of the peripheral pulses was of importance in the diagnosis of coarctation. Femoral pulsations were weak. Although the blood pressure in the arms was not elevated, that in the legs could not be measured. The aortic stenosis, interfering with left ventricular output at a proximal level, discouraged the development of the hypertension in the aortic arch and its vessels which would be present in uncomplicated coarctation.

Assessment of the relative importance of the defects properatively depended upon consideration of the electrocardiogram and the catheterization data. In both patients, there was a pattern of left ventricular hypertrophy. Each of the lesions may cause this. It was obvious that the coarctation did not contribute in these patients because of the lack of hypertension in the arch. In other words, under the circumstances, the coarctation demanded no extra work on the part of the left ventricle. The specific effect of the ductus could not be determined. Flow could have been greater in the past and might have required ventricular hypertrophy. Pulmonary vascular changes taking place over a period of time would then have decreased the shunt. However, the observations in regard to the relative importance of the stenosis and the coarctation indicated that the stenosis must be more important than the ductus.

It followed that relief of the aortic stenosis must be the prime consideration in therapy. If the coarctation were to be resected and the ductus interrupted without relieving the stenosis, the burden on the left ventricle would remain. It was clear, too, that were the stenosis alone attacked there would still be a major and a minor cause of left ventricuar over-

work. It was obvious that all three defects must be corrected during the same operation.

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Atrioventricular Nodal Rhythm with Antegrade Block

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Atrioventricular nodal rhythm is an infrequent, electrocardiographic finding in which the pace-maker has shifted from the sinus node to the atrioventricular node. The characteristic electrocardiographic findings of this rhythm are as follows:[1-6]

1. In the limb leads the P waves are inverted in II, III, and aVF, and are upright in aVR, aVL and I (small amplitude).

2. It is usually associated with bradycardia.

3. The PR interval may vary from 0.12 second to negative value, i.e., an RP interval.

Nodal rhythms are classified as upper, middle, and lower nodal rhythm according to the positions of the retrograde P wave to the QRS wave. This classification is based on the assumption that the impulse originates from a nodal focus and spreads at normal speed in upper and lower directions. If there is some conduction disturbance of the nodal impulse on its way to the auricle (retrograde block) or ventricle (antegrade block), this classification can not be used.[1] A PR interval of more than 0.12 second can be observed in cases of atrioventricular nodal rhythm associated with antegrade block.[1, 3, 6] Because of its rarity, we are reporting an atrioventricular nodal rhythm with antegrade block observed during cardiac surgery and later spontaneously in the post-operative period, in which the auricular conduction was delayed as long as 0.25 second.

Case Report: J. B., a 56 year old white man, was admitted to the City of Hope Medical Center on October 22, 1956. He had developed shortness of breath on exertion

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From the Hospital for Cardiac Disease and The Medical Research Institute, City of Hope Medical Center.

one and one-half years before admission. He also had nocturnal dyspnea, orthopnea, and palpitation which had been treated with digitalis and mercurials with improvement. For several months prior to admission his symptoms worsened. He had no past illness except for Tetanus five years previously.

The blood pressure was 102/90. There were no rales in the chest. The point of maximum impulse was in the left fifth intercostal space at the mid-clavicular line. There was a Grade IV systolic murmur and a palpable thrill at the aortic area which was transmitted into the neck. There was a Grade I to II aortic, diastolic murmur best heard in the left third intercostal space at the sternal border. The liver, kidney, and spleen were not palpable, and there was no peripheral edema.

Laboratory Findings: The laboratory findings including urine, routine blood chemistries, and serological tests for syphilis were within normal limits.

X-ray examination revealed the heart enlarged in its transverse diameter with rounding of the left heart border due to left ventricular hypertrophy. The aorta was elongated with some dilatation distal to the aortic valve. Dense calcification was seen in the region of the valve. The left auricle was also enlarged, displacing the esophagus posteriorly.

A direct blood pressure recording from the brachial artery measured 80/54 mm. of Hg., with a typical aortic stenosis pressure curve. The diagnosis of aortic stenosis with slight degree of aortic insufficiency was made.

An aortic commissurotomy was performed on November 9, 1956. At surgery, marked post-stenotic dilatation of the aorta was found, and a marked systolic thrill was felt in this area. He tolerated the commissurotomy well. However, several days post-operatively, congestive cardiac failure ensued. He failed to respond to increased digitalization, mercurials, etc., and died on the eighth post-operative day, November 16, 1956.

The post-mortem revealed a markedly hypertrophied and dilated right and left ventricle, with a markedly calcified stenotic aortic valve. There was no evidence of myocardial infarction in either ventricle, septum, or in the auricles.

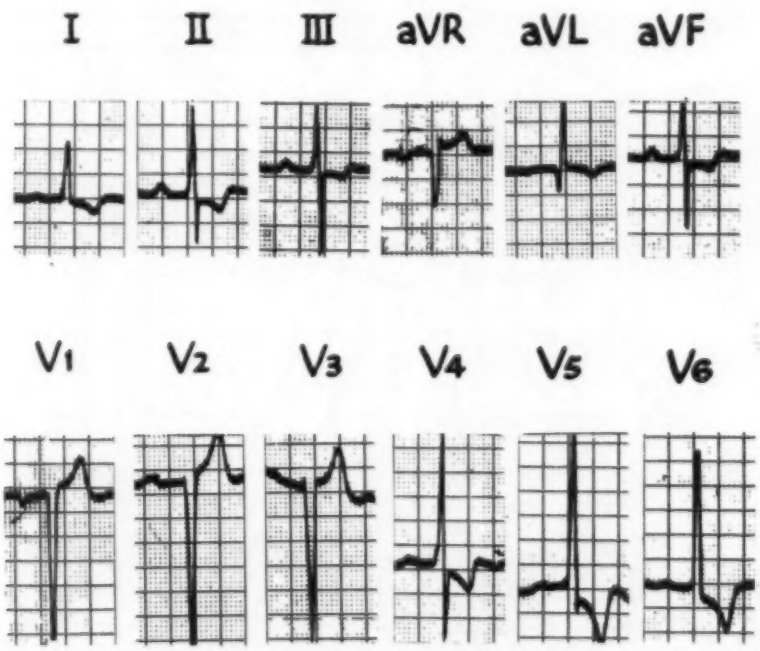

FIGURE 1: Pre-operative electrocardiogram. Note the PR interval 0.26 seconds, and the P wave; upright in Leads I, II, III, aVF, and inverted in aVR and aVL. The ventricular heart rate was 76 per minute.

The first electrocardiographic tracing (Figure 1) taken October 22, 1956, was interpreted as an abnormal electrocardiogram, with left ventricular hypertrophy, first degree atrioventricular block, and digitalis effect and/or myocardial injury and ischemia. The P wave was upright in all the standard limb leads and V_3 through V_6; was inverted in aVR, and diphasic in aVF. The PR interval was 0.26 seconds. The heart rate was regular at 76 per minute.

The electrocardiogram taken on the morning of the operation (November 9, 1956) was essentially the same except for a sinus tachycardia of 107 per minute. Immediately after the chest was entered, auricular fibrillation with a ventricular rate of 150 per minute occurred. In a few minutes normal sinus rhythm was re-established spontaneously with a PR interval of 0.28 seconds (Figure 2A). This change from sinus rhythm to auricular fibrillation to sinus rhythm subsequently occurred six times. After these changes the following interesting alteration occurred. Sharply inverted P waves were observed in Lead II with a PR interval of 0.25 seconds (Figure 2B). After a few minutes, sinus rhythm occurred spontaneously (Figure 2C). These changes recurred three times during the surgery.

The electrocardiogram upon completion of the surgery was the same as preoperatively.

On the second post-operative day, the deeply inverted P wave was again noted in

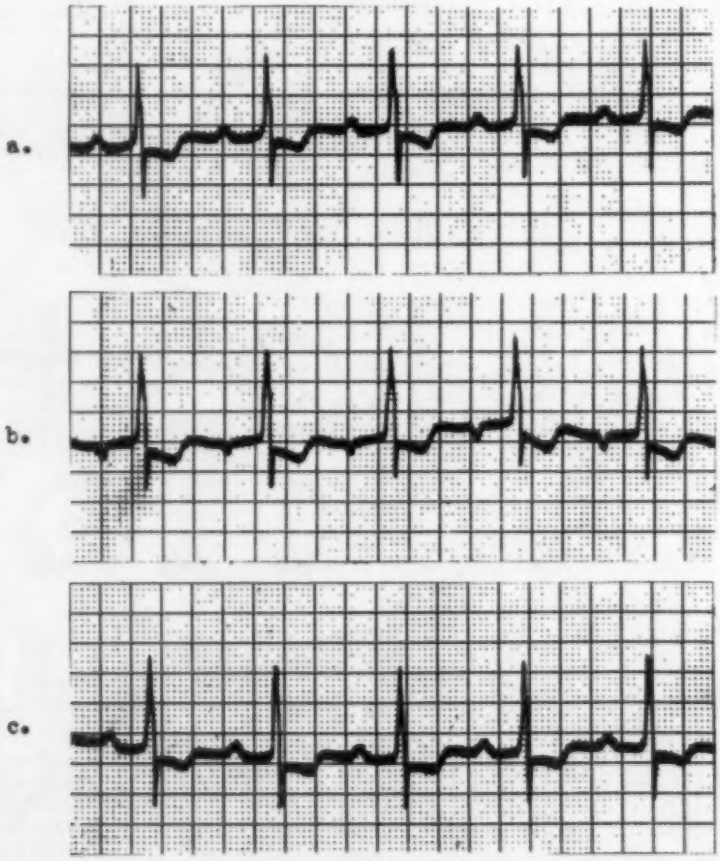

FIGURE 2: Lead II only. (a) at start of surgery, (b) antegrade block, atrioventricular rhythm during surgery, PR interval is 0.25 seconds and (c) spontaneous return to normal sinus rhythm.

Leads II, III, and aVF with an upright P wave in Lead I. aVR and aVL (Figure 3). The chest leads were not taken because of the operative wound. The PR interval in Lead II was 0.22 seconds.

On the following day auricular fibrillation recurred and persisted.

DISCUSSION

The outstanding features of this case are the sharply inverted P waves in Lead II, III, aVF and marked prolongation of the PR interval. Before the shift of the pace-maker from the sinus to the atrioventricular node, this patient had evidence of disturbance of auricular conduction as demonstrated by a first degree A-V block with a normal sinus rhythm.

Langendorf and co-worker[1] concluded that the classification of atrioventricular nodal rhythm as upper, middle, and lower nodal rhythm is not suitable in the presence of atrioventricular block. Retrograde (depression of the impulse conduction to the auricle) will shorten the PR in-

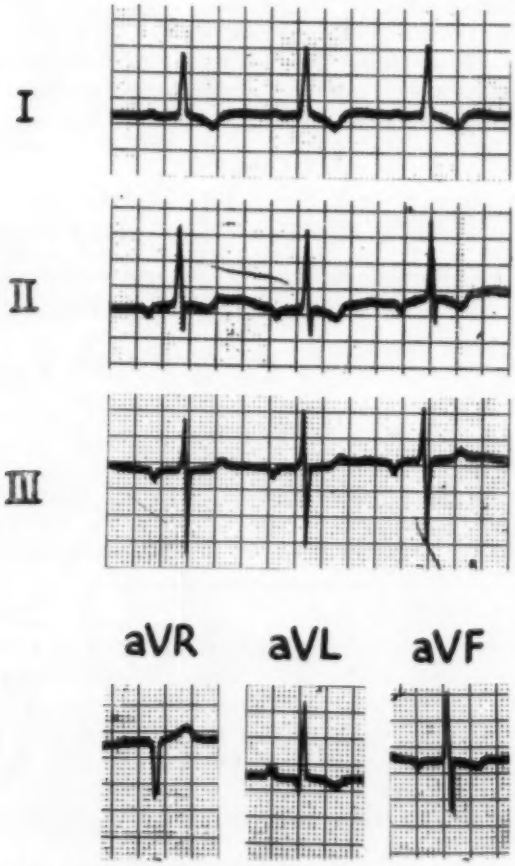

FIGURE 3: Limb leads taken on second post-operative day. The rate is 72 per minute. P is upright in 1, aVR, aVL, inverted in II, III, aVF. PR internal is 0.22 seconds.

terval and tend to convert it into an RP interval. Antegrade block (depression of the impulse conduction to the ventricle) will prolong PR interval and tend to convert an RP into a PR interval. They reported one case with antegrade block, the PR interval measuring 0.18 sec.

Vakil[3] reported two cases of atrioventricular nodal rhythm with antegrade block. One of them, an elderly, hypertensive patient with acute pulmonary edema, had a PR interval of 0.16 second. The other patient showed three different types of rhythm besides normal sinus rhythm, namely (a) uncomplicated upper nodal rhythm, (b) nodal tachycardia with two to one atrioventricular antegrade block, and (c) nodal tachycardia with instances of two to one block, first degree heart block and nodal pause. The PR interval of the case was 0.09-0.10 sec. One complex showed a PR interval of 0.20 sec. followed by retrograde P wave.

Bix[6] reported three interesting cases of nodal rhythm with A-V block. One of them showed A-V nodal rhythm with A-V block in form of Wenckebach phenomenon.

The electrocardiogram of our patient showed A-V nodal rhythm with antegrade block, in which PR interval measured 0.25 seconds. This is a larger PR interval associated with atrioventricular nodal rhythm with antegrade block than we could find in any other paper.

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An Unusual Cause of Massive Hemothorax

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New York, New York

Although intestinal obstruction and strangulation as a complication of traumatic diaphragmatic hernia are well recognized and have been reported frequently since the first case was described by Pare in 1564,[1] massive bloody pleural effusion has been seldom associated with strangulation. The paucity of the symptoms referred to the abdomen in this case is most unusual.

O. M., a 33 year old colored man, was admitted on December 9, 1954, complaining of shortness of breath and swollen abdomen.

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**Chief Resident in Medicine, City Hospital. (Fulbright Scholar from Iraq)

He had led an apparently uneventful existence with no serious illness until one week prior to admission when he developed a "cold" followed by cough productive of about an ounce of mucoid sputum daily. Five days prior to admission he experienced a sharp pain over the lower and lateral part of the left chest, which was aggravated by cough and deep inspiration. This condition progressively deteriorated and he developed increasing shortness of breath. He became aware of abdominal swelling in the last two days. The last bowel movement occurred two days prior to admission to the hospital. He experienced no abdominal pain or vomiting. Interrogation revealed that abdominal distension had occurred on many occasions in the past and had been relieved by infrequent bowel movements.

He was a moderate smoker but had over-indulged in alcoholic beverages for the past 10 years.

Physical examination revealed an acutely and extremely ill individual in severe respiratory distress, sweating profusely. The facial expression was anxious and apprehensive. The pulse rate was 120 per minute, regular but of low volume. Rectal temperature was 101.2° F., and respiration attained a rate of 40 per minute and was shallow in character.

Examination of the eyes, ears, nose and throat revealed an essentially normal status except for slight hyperemia of pharyngeal mucosa. There was marked deviation of the trachea toward the right. There was no evidence of clubbing of the finger tips and no lymphadenopathy was palpable anywhere in the body. There were old healed scars on the face, left arm and in the left eighth intercostal space at the scapular line. The expansion of the left hemithorax was markedly limited.

Palpation revealed diminished tactile fremitus over the entire left hemithorax. Percussion elicited flatness over the same side except at the extreme apex. The apex beat was palpable in the right fourth intercostal space two inches to the right of the sternal border. Percussion of the cardiac dullness confirmed the palpatory finding. On auscultation the heart sounds were regular, rapid and best heard over the right hemithorax. The expiratory phase of respiration was prolonged and there were diffuse expiratory wheezes over the right lung. The breath sounds were faint and distant over the left hemithorax except at the apex.

The abdomen was moderately and uniformly distended but no tenderness or rebound tenderness could be elicited. Peristalsis was hypoactive.

Rectal examination and the remainder of the physical examination were unremarkable.

Laboratory findings were red blood cells 4,600,000 per cubic millimeter, hemoglobin 11 grams per cent, hematocrit 33 per cent, white blood cells 21,800 per cubic millimeter with shift to the left. Urine was normal. Serum analysis of the blood was 6 Winslow's units.

An x-ray film of the chest revealed a homogeneous density involving the entire left hemithorax. There was marked mediastinal shift toward the right. The dome of the left diaphragm could not be visualized. The findings were consistent with massive pleural effusion (Figure 1).

Thirty-three hundred cubic centimeters of grossly bloody fluid was aspirated from the left pleural space. The fluid had the appearance of thin dark venous blood. The hematocrit on this fluid was 5 per cent and it contained 460,000 red blood cells per cubic millimeter. The serum analysis value of the aspirated material was 4 Winslow's units. During thoracentesis, 1,000 cc. of blood were transfused to the patient, which raised the hematocrit from 33 to 39 per cent.

He improved subjectively and objectively following thoracentesis and transfusion. A subsequent x-ray film demonstrated that the upper limit of the homogeneous density in the left hemithorax had descended to the level of the fourth costal cartilage anteriorly. A large circumscribed area of radiolucency in the left apex, which was interpreted as localized pneumothorax, was visualized. The mediastinum returned to a median position; the dome of the left diaphragm was still not demonstrable (Figure 2). X-ray examination of the abdomen showed a small and large bowel distension with fluid levels (Figure 3).

Abdominal decompression was attempted by continuous Wangensteen suction. Nothing was given by mouth but intravenous fluids were administered together with wide range antimicrobial drugs.

Surgical consultation resulted in the opinion that the abdominal distension was due to paralytic ileus. Normal saline, soap and water and warm olive oil enemas were unsuccessful and the abdominal distension was unaffected by attempts at oral and rectal decompression.

He developed a coarse tremor of the hands and lips and was incoherent and irrational. By the second hospital day he was in frank "delirium tremens."

X-ray film of the chest on the third hospital day revealed diminution of the density

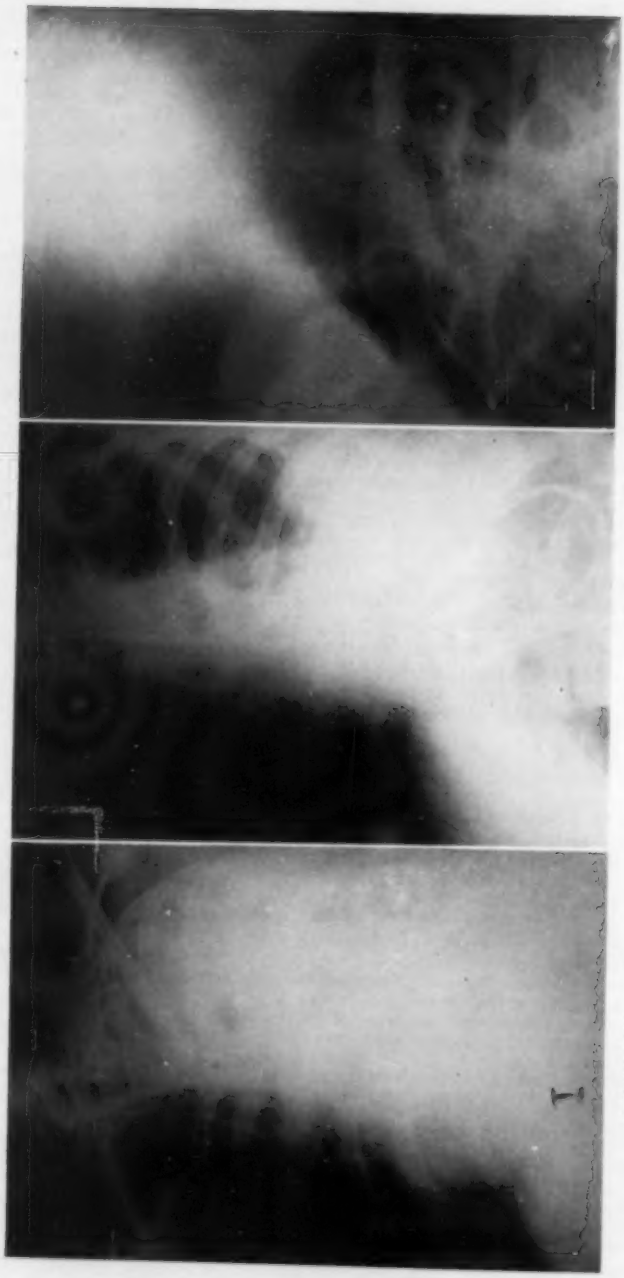

FIGURE 3

FIGURE 2

FIGURE 1

in the left chest. The left diaphragm was still not visualized but two fluid levels were seen in this area (Figure 4).

Seventy-two hours after admission, for the first and last time he vomited coffee ground material and expired 15 minutes later. The fluid aspirated from the chest was reported after death to be positive for anaerobic streptococci and E. coli on culture.

Autopsy showed abdominal distension. Old healed scars were present on the face, left arm and a third one, two inches in length, along the left eighth intercostal space in the scapular line. The gastrointestinal tract was markedly distended and covered with sero-fibrinous exudate. The descending colon was empty and collapsed below the splenic flexure.

The lungs revealed emphysematous changes in the upper lobes with emphysematous bullae in the apex of the left lung. The remainder of the left lung was atelectatic and covered by sero-fibrinous exudate and was firmly attached to the chest wall antero-laterally.

A loop composed of splenic flexure and part of the transverse colon was found in the left hemithorax. The loop was found to be edematous, hemorrhagic and necrotic. There was no peritoneal sac to this loop. The diaphragmatic opening was in the postero-lateral position of the left diaphragm. It was small with an organized plastic fibrous ring.

Microscopical examination of the strangulated loop showed destroyed mucosa with polymorphonuclear cell infiltration and fibrin deposition.

Discussion

Intestinal obstruction and strangulation are not infrequent complications of diaphragmatic hernia and are the most dangerous ones indeed. About 90 per cent of all cases of strangulated diaphragmatic hernia are traumatic.[2] Almost all the cases reported, or 98.4 per cent are left sided[3] for obvious anatomical reasons.

Pleural effusion accompanying strangulation of herniation through the diaphragm is not an unusual finding and has been detected clinically, radiologically, through thoracotomy, or at autopsy, on many occasions. The character of the fluid may be serous[4] but is often serosanguinous because of the underlying physio-pathology.

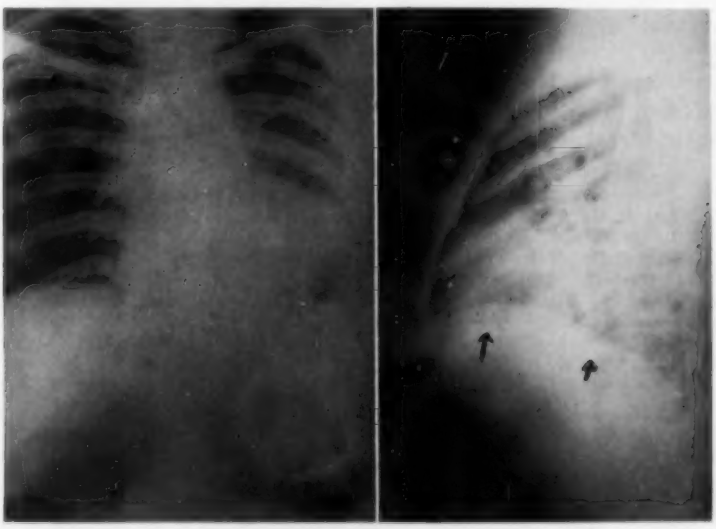

FIGURE 4

Although bloody pleural effusion was described as early as 1858 as a fortuitous finding by Alderson during an autopsy of a case of strangulated diaphragmatic hernia with perforation of the stomach,[5] massive hemothorax has been rarely encountered or reported.

We were able to find only three cases in the literature more or less comparable to the case being reported in respect to the amount and character of the pleural effusion.[2,6,7]

Deaner et al[8] described a case of hemothorax with strangulated diaphragmatic hernia with opacification of the left chest on x-ray film but the amount of fluid aspirated was only 37 cc. on two occasions. On autopsy the left hemithorax contained omentum and clotted blood.

However, this case is unique and different from all the cases previously reported in the paucity of abdominal symptoms and signs except for the distension which, together with the sluggish peristalsis and the absence of pain and vomiting, had been attributed to paralytic ileus.

In all the cases reported, the abdominal symptoms of pain, discomfort and vomiting were the predominant part of the clinical picture. Although chest pain, dyspnea and evidence of pleural effusion are common with strangulated diaphragmatic hernia, they have apparently never been so overwhelmingly the outstanding part of the clinical picture as to effectively mask the abdominal component.

The history of a "cold" as the onset of the present illness, the diffuse wheezing and evidence of bronchospasm, the presence of radiolucency which was interpreted as localized pneumothorax or a bulla, the massive bloody pleural effusion, the absence of abdominal pain, vomiting or tenderness, the sluggish peristalsis, in addition to complicating delirium tremens, directed attention to the respiratory system as the site of primary pathology.

Barium enema to investigate the cause of abdominal distension probably would have given the answer and would have resulted in the correct surgical approach to the problem. The patient expired before the clue given by the report of the culture of the pleural effusion was received and before further studies could be initiated.

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Artificial Pneumothorax in the Treatment of Pulmonary Tuberculosis Case Reports

HANS KUMAR, M.B., B.S., F.C.C.P.*
Jaipur, India

Pneumothorax was the first effective form of collapse therapy to be used widely. During the first 40 years of the present century, it attained world-wide acceptance, becoming at one time the standard and almost universally preferred method of pulmonary collapse. During recent years, its popularity has diminished to a marked degree especially in the United States; some large Tuberculosis Institutions having abandoned it completely. In this hospital, we do not use pneumothorax as a routine therapeutic procedure, our patients are treated on pneumoperitoneum and chemotherapy followed by major chest surgery. However we do feel that in some circumstances, no other measure is likely to be useful and the following case reports are presented with that object.

Case 1: This 22 year old man was admitted to the hospital with severe hemoptysis but gave no previous history of tuberculosis. An x-ray film on admission showed evidence of exudative infiltration with break down in the right upper zone (Figure 1). Absolute rest, sedation with morphia and coagulants were given along with chemotherapy but recurrent and profuse hemoptysis continued. His condition deteriorated and he became moribund: Artificial pneumothorax on the right side was induced and the hemoptysis stopped immediately. X-ray film showed collapse of right lung with apical adhesion. He has improved clinically and is advised to undergo pulmonary resection.

Case 2: This 30 year old man was admitted with far advanced bilateral pulmonary tuberculosis more extensive in the left upper and mid zone (Figure 2). He was treated on bed rest, pneumoperitoneum and chemotherapy. After nine months he did not show radiological improvement; recurrent hemoptysis started and his general condition gradually deteriorated. To stop hemoptysis, artificial pneumothorax was induced on the left side. This did not permit complete relaxation of the diseased area but produced sufficient alteration of intrapulmonary mechanics to stop bleeding. His general condition improved, there was no recurrence of bleeding, his disease on the contralateral side regressed and a seven rib thoracoplasty was done on the left side.

Though artificial pneumothorax is not often used in the treatment of hemoptysis, the above two cases remind us that it may be valuable and its use should not be relegated entirely to the realms of history.

Case 3: This case demonstrates indication of pneumothorax in cases where pneumoperitoneum and chemotherapy has failed to close cavities in patients in whom the lesion is not considered more suitable for resection or surgical collapse.

This 35 year old man was admitted with bilateral advanced pulmonary tuberculosis with multiple cavities in the left lung. Treatment with pneumoperitoneum, bed rest and chemotherapy for one year failed to bring radiological improvement, the cavities persisted and the disease with contralateral lung did not show regression (Figure 3). His general condition was poor and he was producing a large amount of sputum positive for acid fast bacilli. Pneumothorax was induced on the left side and the adhesions were cauterized by closed intrapleural pneumonolysis (Figure 4). His general condition has improved, sputum is negative for acid fast bacilli and the disease in the contralateral lung has regressed. He is now ready to undergo major chest surgery.

*Medical Superintendent, Tuberculosis Sanatorium.

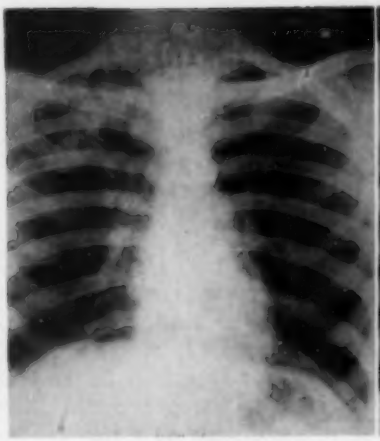

FIGURE 1

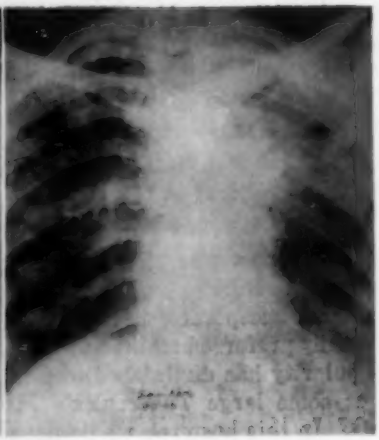

FIGURE 2

Figure 1: Exudative infiltration with breakdown right upper zone.—*Figure 2:* Left upper and mid zone extensive disease with cavities. Right mid zone disease with cavity.

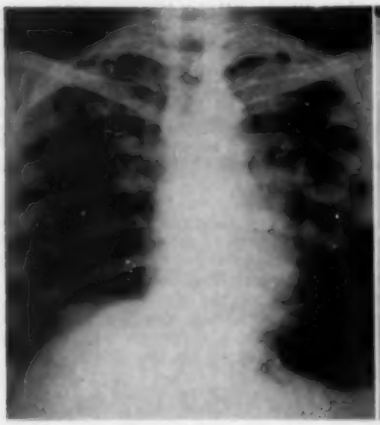

FIGURE 3

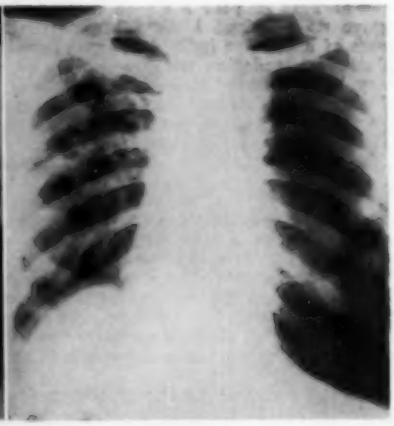

FIGURE 4

Figure 3: Left upper and mid zone cavity persists. No change in disease elsewhere.—*Figure 4:* Collapse left side—Upper lobe well collapsed.

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The Meaning of International Congresses

As a participant in and as one of the organizers of the international congresses on diseases of the chest held in Rome, Italy, in 1950; Rio de Janeiro, Brazil, in 1952; Barcelona, Spain, in 1954; and in Cologne, Germany, in 1956; I have had ample opportunity to appraise critically their role and value in world affairs.

These congresses were organized under the sponsorship of the American College of Chest Physicians. The College, a symbol of lofty ideals in the healing arts, has been a leader in the international development of undergraduate and postgraduate medical education, and a standard bearer in the dispersement of scientific knowledge.

These congresses evolved from the desire for better international understanding and good will. It should not be surprising, therefore, that they have received universal approbation of the medical profession of the world. Thus, these congresses occupy a rightful, permanent place in medical events and are used as models by other groups. These congresses make possible the prompt and maximal dissemination of important scientific news.

The scientific program to be presented at the Fifth International Congress on Diseases of the Chest in Tokyo, September 7-11, will cover many surgical and clinical aspects in the treatment of chest diseases. Tuberculosis and carcinoma of the lung, other infections, diseases of allergic origin, thoracic trauma, occupational disorders, parasitic infestations, tropical ailments, hazards of radio-active fall-out, pediatric cardiology, cardiorespiratory problems of the postnatal period and in geriatrics, will be included. Special attention will be paid to emphysema, metabolic and other systemic affections involving the lungs and heart. Due time will be devoted to diseases of the esophagus, mediastinum and the diaphragm, as well as to recent advances in diagnostic methods, including cytology, the use of isotopes and to cardiology. Consideration will be given to modern procedures in the use of antibiotics, chemotherapy, aerosols and physical therapy, with emphasis on rehabilitation of the respiratory invalid and the cardiac cripple. Aviation medicine and its anticipated interplanetary problems is of immense interest and demands due thought. Of course, the tremendous strides in thoracic and cardiac surgery require ample time commensurate with their importance.

In accordance with plans, eminent clinicians and research workers will participate in the transactions of the congress in formal lectures, fireside conferences, and in panel discussions. You are likely to hear some animated, spirited debates on these occasions.

The program will be augmented by scientific motion pictures and scientific and technical exhibits which are highly instructive.

What is the explanation of the unprecedented success of the international congresses of the College? It is axiomatic that the value of human life to the individual is the same in the lowest as in the highest socio-economic strata of society; it is the same in small countries as in

large ones; it is the same in the temperate zone as it is in the tropics or at the Arctic. Obviously, as long as disease remains the common enemy of mankind, as long as it spreads in global dimensions—as we have witnessed recently in the form of Asian influenza—it is unwise to confine medical science within regional or national boundaries. Scientific isolationism cannot be condoned. It is deplorable from the viewpoint of all ethical standards of medicine. Actually, its fallacious egotism hurts the isolationists themselves no less than it hurts the welfare of their patients.

The international congress offers a wonderful occasion for meeting doctors of all nationalities. Psychologically, contact with others is destined to dispel fear, reserve and the admittedly primitive but powerful instinct of "dislike of the unlike." No doubt, these international conventions are the best antidote for discrimination and prejudice.

If you attend with an open and receptive mind, you cannot fail to realize that the scientific discoveries presented by notable pioneers arouse a desire for an accelerated tempo of inquisitiveness toward hitherto unfathomed health problems. Veritably, a congress of this sort imparts catalytic influences in inspiration and awareness. Ideas gathered there are likely to sharpen one's focus on relevant entities, set into motion new trends of thoughts and may rectify vague notions and reveal flaws in our own seemingly accurate reasoning.

Of course, there is a lighter side to the congress too. The warm hospitality of our hosts and their proverbial generosity will leave a lasting impression. Needless to say, there will be the enchanting, picturesque scenic beauty of Japan. When, at the conclusion of the meetings, you bid adieu, you will leave the congress with worthwhile scientific knowledge and with cherished, warm sentiments for new friends.

ANDREW L. BANYAI, M.D., F.C.C.P.*
Milwaukee, Wisconsin

*Chairman, Council on International Affairs.

The President's Page

For the past six months the College journal has been publishing a series of articles concerning the physicians' role in promoting world peace. Prominent physicians in various parts of the world have contributed to this splendid series of editorials. Our Editor, Dr. Jay Arthur Myers, who initiated the series, wrote the first editorial which appeared in the September 1957 issue. No doubt other members of the College have thoughts on this important subject and I am sure that the Editorial Board would be pleased to consider articles if they wish to submit them. World peace is of vital importance to everyone and the physician, who is concerned with life itself, must play an important part.

I should like to call your attention to the Section on Cardiovascular Disease, which started with the January issue of the journal. This section was introduced because of the diversified interests of our members and the large number of members who specialize in cardiology. The Editorial Board would like to have your comments on the series of articles dealing with "Current Therapy in Cardiovascular Disease" and the "EKG of the Month." Contributions to these special sections may be submitted for consideration by the Board.

Plans for the 24th Annual Meeting of the College to be held in San Francisco, June 18-22, are progressing satisfactorily. The program will be published in the April issue of *Diseases of the Chest* and I know that all of our members will want to be present for these exceptionally fine scientific sessions.

The councils and committees of the College will hold their annual meetings at the Fairmont Hotel, San Francisco, on Thursday, June 19, and it is expected that all members will be present. Our councils and committees will function effectively only if all members attend the meetings and contribute to their respective programs.

I must call your attention once again to the fact that the hotel situation in San Francisco is critical. Members who plan to attend the annual meeting and who have not made their hotel reservations are urged to do so at once. A reservation coupon appears on page xxxii of this issue of the journal.

The Committee on Nominations, composed of Dr. J. Winthrop Peabody, Washington, D. C., Chairman, Dr. Sumner S. Cohen, Oak Terrace, Minnesota, and Dr. Orin J. Farness, Tucson, Arizona, will be pleased to receive recommendations from members of the College for officers to be elected at the coming annual meeting.

There is a great deal of enthusiasm among our members throughout the world regarding the Fifth International Congress to be held in Tokyo, Japan, September 7-11, 1958. The Congress is being presented under the Patronage of the Government of Japan with Prime Minister Nobusuke Kishi as the Honorary President. The College chapters in Japan, Hong Kong, the Philippines and Hawaii are planning special scientific and social programs in connection with the Congress in Tokyo. If you are planning to attend and have not yet made arrangements, I strongly urge you to communicate with the Executive Offices of the College in Chicago and they will be pleased to assist you.

Burgess L. Gordon

SEVENTH INTERNATIONAL CONGRESS ON BRONCHOESOPHAGOLOGY

The International Bronchoesophagological Society will hold its Seventh International Congress in Kyoto, Japan, September 12-14, 1958, immediately following the Fifth International Congress on Diseases of the Chest in Tokyo, September 7-11. A group of physicians and their families attending the Tokyo congress will travel to Kyoto to attend the Bronchoesophagological Congress. A number of prominent physicians will participate in the scientific program at the Kyoto meeting. The preliminary program is as follows:

September 12—President's Reception (8:00 p.m.)

September 13—Morning Scientific Session
Luncheon by courtesy of the Mayor of Kyoto and the Prefectural Governor
Afternoon sightseeing tour
Banquet (7:00 p.m.)

September 14—Morning Scientific Session
Luncheon by courtesy of the Mayor of Nara and the Prefectural Governor
Sightseeing tour of Nara
Farewell Party by the President of the Congress in Kyoto

There will also be entertainment for the members and their ladies including the Kyoto Dancing Girls, pottery making, a visit to a brocade factory, deer calling, shooting the rapids, and other features characteristic of Kyoto and Nara.

For registration and further information please address Dr. Chevalier L. Jackson, Executive Secretary-Treasurer, International Bronchoesophagological Society, 3401 North Broad Street, Philadelphia, Pennsylvania.

College Chapter News

ALABAMA CHAPTER

The Alabama Chapter will hold its annual meeting in Montgomery just prior to the meeting of the Alabama Medical Society, April 17-19. The chapter meeting will be held at the Whitley Hotel, starting at 2:30 p.m. on Wednesday, April 16, and the following program will be presented:

Chairman: Arthur Calix, Decatur

"Pulmonary Emphysema, Modern Concepts Relative to Its Diagnosis and Treatment of this Disabling Disease"
Ben Branscomb, Birmingham

"Cardiac Arrest as a Complicating Factor in the Performance of Major Surgery"
Rex Perkins, Birmingham

"Byssinosis, A Review of the Literature Pertaining to This Disease Commonly Found in Residents of Alabama"
William J. Talley, Gadsden

"The Treatment of Cardiospasm"
David H. Waterman, Knoxville, Tennessee

A social hour will be held at the Whitley Hotel from 5:00 to 6:00 p.m. by courtesy of the Durr Drug Company.

CALIFORNIA CHAPTER

The California Chapter will hold its annual meeting at the Ambassador Hotel, Los Angeles, on April 26, in conjunction with the California Medical Association meeting, April 27-30.

GEORGIA CHAPTER

The annual meeting of the Georgia Chapter of the College will be held in conjunction with the annual meeting of the Georgia Medical Association on Tuesday, April 29, at the Macon Auditorium, Macon, Georgia. The guest speaker will be Dr. Paul T. Chapman, Detroit, Michigan, Director of the Tuberculosis Division, Herman Kiefer Hospital. Dr. Chapman will speak on "Acute Suppuration and Tuberculosis" at 10:30 a.m. Following Dr. Chapman's lecture, a luncheon and business meeting of the Chapter will be held in the S & S Cafeteria in Macon.

ILLINOIS CHAPTER

The Illinois Chapter of the College will hold a joint meeting with the Illinois Trudeau Society at the Faust Hotel, Rockford, Illinois on April 24.

LOUISIANA CHAPTER

The Louisiana Chapter of the College will hold its semi-annual (spring) meeting on April 12 at the Bellemont Motel, Baton Rouge. The scientific program is as follows, opening at 2:00 p.m.

Panel I—The Diagnosis and Management of Congenital Heart Disease
Moderator: Richard Fowler, New Orleans
Panelists: Page Acree, Baton Rouge
John Stotler, Baton Rouge
David Van Gelder, Baton Rouge

Panel II—Obstructive Diseases of the Esophagus
Moderator: Charles Beskin, Baton Rouge
Panelists: R. C. Boyer, Baton Rouge
Louis Ochs, New Orleans
Dennis Rosenberg, New Orleans

Panel III—Granulomatous Diseases of the Lung
Moderator: Dwight Danburg, Baton Rouge
Panelists: Walter McCook, Shreveport
Albert McQuown, Baton Rouge
John Seabury, New Orleans

5:00 p.m.—Business Meeting
6:00 p.m.—"Dutch Treat" Buffet Supper

PACIFIC NORTHWEST CHAPTER

The following officers were elected at the annual meeting of the Pacific Northwest Chapter held in Portland, Oregon, November 8-9, 1957:

President:	William G. Trapp, Vancouver, B. C., Canada
Vice-President:	Kenneth A. Tyler, Gooding, Idaho
Secretary-Treasurer:	Donald A. Campbell, Tranquille, B. C., Canada

TENNESSEE CHAPTER

The Tennessee Chapter of the College will hold its annual meeting at the Riverside Hotel, Chattanooga, on Monday, April 21. The meeting will open with a luncheon at 12:00 noon, to be followed by a business meeting at 1:00 p.m. The scientific program is as follows:

"Bronchial Adenoma"
John Carter, Chattanooga

"Problems and Pitfalls in Selection of Patients for Cardiac Surgery"
Frank London, Knoxville

"Cardiospasm"
David H. Waterman, Sheldon E. Domm, and William K. Rogers, Knoxville

"Blood Loss in Surgery"
J. C. Lougheed, Memphis

"Dehisence of the Diaphragm Associated with Fractures of the Pelvis or Lumbar Spine Due to Non-Penetrating Wounds of the Chest and the Abdomen"
R. I. Carlson, W. G. Gobbel Jr., Walter L. Diveley, and R. A. Daniel Jr., Nashville

"Pulmonary Embolism"
Ira T. Johnson, Hollis E. Johnson, and Thomas B. Holton, Nashville

"Case Presentations with X-Ray Records"
John M. Crowell, Chattanooga

MISSOURI CHAPTER

The Missouri Chapter will hold its annual meeting at a luncheon on Sunday, April 13, at the Statler Hotel, St. Louis. Dr. Duane Carr, Memphis, Tennessee, will be guest speaker.

PHILIPPINE CHAPTER

The Philippine Chapter of the College held a special dinner meeting at the Club Filipino in Manila on November 2, 1957, during the visit of Mr. and Mrs. Murray Kornfeld (see photograph). Mr. Kornfeld addressed the meeting on the subject "The College as an International Force in the Interests of Science and World Peace." Approximately 100 members of the College in the Philippine Islands attended this special meeting. Plans for the attendance of a large delegation of members from the Philippines to the Congress in Tokyo next September were discussed and it is also planned to have a post-congress meeting in Manila, sponsored by the Philippine Chapter of the College. Dr. Miguel Canizares, Regent of the College for the Philippines, will be in charge of the arrangements.

While in Manila, Mr. Kornfeld visited the Quezon Institute where a luncheon meeting was held, attended by the officers of the Philippine Chapter. He also paid his respects to Mrs. Magsaysay, the widow of the late President of the Philippine Islands.

1st Row, Left to Right: Dr. Priscilla Tablan, Secretary-Treasurer, Philippine Chapter, Dr. Godofredo Hebron, President, Philippine Chapter, Dr. Miguel Canizares, Regent for the Philippines, Mr. Murray Kornfeld, Executive Director of the College, Dr. Manuel A. Quisumbing, Governor for the Philippines, Dr. Horace de Lien, Director of Public Health Division, Mutual Security Agency, Special Technical and Economic Mission to the Philippines.
2nd Row, Left to Right: Dr. Sixto A. Francisco, Dr. Soledad Florendo, Dr. Sofia Bona, Dr. B. Valdes, Dr. B. Canaga, Dr. In. P. de Tavera.

BARCELONA (SPAIN) CHAPTER

The Barcelona Chapter of the American College of Chest Physicians will hold a scientific meeting in Zaragoza, March 31-April 1, 1958. All physicians are cordially invited to attend.

TEXAS CHAPTER

The annual meeting of the Texas Chapter will be held in Houston on April 20, in conjunction with the Texas State Medical Association meeting, April 20-23. The following program will be presented.

9:00 a.m. Lawrence M. Shefts, San Antonio, presiding
"Bronchogenic Carcinoma in Routine Tuberculosis Hospital Admissions"
Ellison F. White, Harlingen, and Carlos J. Quintanilla, San Antonio
"Observations on Quarantine Patients"
James P. Hodges, San Antonio
"Fungus Skin Testing of Routine Admissions to a Tuberculosis Hospital"
Edmund Rague, Kerrville
"Allergic and Toxic Reactions of Prolonged Chemotherapy for Pulmonary Tuberculosis"
Bernard T. Fein, San Antonio
Panel Discussion on "Treatment of Tuberculosis"
David McCullough, San Antonio, Moderator
A. Wilson Harrison, Galveston
Lloyd R. Hershberger, San Angelo
John W. Middleton, Galveston
Jack Miller, Galveston
Samuel Topperman, Tyler

12:30 p.m. Luncheon and Business Meeting
Remarks: Burgess L. Gordon, Albuquerque, New Mexico President, American College of Chest Physicians

2:00 p.m. John A. Wiggins, Ft. Worth, presiding
Charles M. Hendricks Memorial Lecture
"The Problems of Chronic Pulmonary Conditions in Older People"
Burgess L. Gordon, Albuquerque, New Mexico
"Mediastinal Tumors"
J. Walter Park III, San Antonio
"Ivalon Sponge Plombage and Prosthesis"
James E. Dailey, Houston
"Resection for Pulmonary Tuberculosis in Patients Over 50 Years of Age"
Clyde E. Rush, Sanatorium

ARGENTINE CHAPTER

The Argentine Chapter of the College met in Concordia on November 10, 1957. The themes discussed were "Treatment of Pulmonary Suppurations" (Non-tuberculous with the exception of bronchiectasis) and "The Use of the Corticosteroids and ACTH in the Treatment of Tuberculosis." Following the scientific session, the following officers were elected:

President:	Oscar Izaguirre, Parana
Vice-President:	Isaac Wolaj, Cordoba
Secretary-Treasurer:	Enrique C. R. Bonfils, Parana

CANARY ISLANDS (SPAIN) CHAPTER ORGANIZED

On November 2, 1957, the Canary Islands Chapter of the College was officially organized during a meeting held by the Barcelona Chapter in Palma de Mallorca. The following officers were elected:

President:	Camilo Rodriquez Gavilanes, Las Palmas
Vice-President:	Jose M. del Arco Montesinos, Sta. Cruz de la Palma
Secretary:	Santiago Enrique Gonzalez, La Laguna
Treasurer:	Jose J. Perez Perez, Sta. Cruz de Tenerife

Arrangements for the meeting were made by Dr. Antonio Caralps, Barcelona, Regent of the College, and Dr. Tomas Cervia, Tenerife, Governor of the College for the Canary Islands.

PENNSYLVANIA CHAPTER

The Pennsylvania Chapter of the College will hold a Clinical Session at the Reading Hospital, Reading on Wednesday, April 16. The following program will be presented:

10:30 a.m. "Shall We Treat the Tuberculin Converter?"
David A. Cooper, Philadelphia
Discussor: John H. Bisbing, Reading
Report of the 17th VA-Armed Forces Conference on Chemotherapy of Tuberculosis
Carl W. Tempel, Valley Forge
"An Evaluation of Chemotherapy in Pulmonary Tuberculosis; High Doses of INH with PAS and Pyridoxine
Stephen J. Berte, Valley Forge
Discussor: Robert L. Mayock, Philadelphia
"Progress in the Diagnosis of Left Heart Lesions"
Don Fisher, Pittsburgh
Discussor: Gordon Myers, Harrisburg

1:00 p.m. Luncheon

2:00 p.m. "The Surgical Management of Pulmonary Emphysema"
John M. Snyder, Bethlehem
Discussor: William DeMuth, Carlisle
"Pulmonary Embolism as a Cause of Massive Pleural Effusion"
Albert L. Sheffer, Dick D. Harrell and Harold L. Israel, Philadelphia
Discussor: Katharine R. Boucot, Philadelphia
"Complacency Concerning Chest Diseases"
Howard Witmer, Lancaster

OHIO CHAPTER

The annual meeting of the Ohio Chapter will be held at the Netherland Plaza Hotel, Cincinnati, on Wednesday, April 16.

PANAMA CHAPTER ORGANIZED

The organizational meeting of the Panama Chapter of the College was held in Panama City on February 13. Dr. Maximo Carrizo Villarreal, Colon, serves as Regent of the College for Panama and Dr. Rodolfo V. Young, is Governor. The following chapter officers were elected:

President:	Alberto Calvo, Panama City
Vice-President:	Octavio Ferrari Jr., Panama City
Secretary-Treasurer:	Antoine Raymundo, Panama City

College News Notes

Dr. Jerome R. Head, Chicago, Illinois spoke on "Philosophy and Medicine" on February 25 in Northwestern University Medical School's lecture series on "The Growth of Medicine" at the medical school.

Dr. Milton M. Hurwitz, St. Paul, Minnesota, was recently elected President of the Minnesota Heart Association.

The following members of the College have recently been certified in the Sub-specialty of Pulmonary Diseases by the American Board of Internal Medicine; **Dr. Virgil A. Plessinger,** Cincinnati, Ohio; **Dr. Edgar A. Riley,** New York City; **Dr. Gordon L. Snider,** Chicago, Illinois. **Dr. W. W. Coulter,** Jr., of Lafayette, Louisiana, has received his certificate in Internal Medicine.

Dr. Oglesby Paul, Chicago, Illinois lectured on "Diet and Diuretics in Congestive Heart Failure" at St. Mary of Nazareth Hospital, Chicago, January 3.

Dr. Roscoe C. Giles, Assistant Professor of Surgery at Chicago Medical School was a recipient of the citation given as outstanding Chicago citizen by the Jesuit Centennial Committee on December 12.

Dr. Harry Isaacs was honored at a dinner on November 30, initiated by members of the Department of Medicine at Chicago Medical School in recognition of his retirement as head of that department.

Dr. H. C. Jernigan, director at large, National Tuberculosis Association Board of Directors has been appointed medical director of the Fort Staunton Tuberculosis Hospital, Fort Staunton, New Mexico.

Dr. Clare Miller, Medical Director of Hillcrest Sanatorium, Quincy, Illinois for the past 27 years, resigned in October.

Dr. George E. Burch, New Orleans, Louisiana, was an out-of-state speaker at the 10th Annual Clinical Assembly of the Arkansas Chapter of the American Academy of General Practice at Little Rock, Arkansas, October 16-17, 1957.

Brigadier General Carl W. Tempel, U. S. Army, Commanding General of Valley Forge Army Hospital, Phoenixville, Pennsylvania, was one of six medical leaders who were honored by the Association of Military Surgeons of the United States at its meeting in Washington, D. C., October 30, 1957.

Dr. Howard F. Root, Boston, Massachusetts, was an out-of-state speaker at the 9th Annual Scientific Assembly of the Maryland Academy of General Practice at Easton, Maryland, October 9-10, 1957.

Dr. Paul Dudley White, Boston, Massachusetts, was a speaker at the 9th Annual Symposium on Heart Disease sponsored by the Washington State Department of Health and the Washington State Heart Association, held at Seattle, October 4-5, 1957.

Dr. George F. Evans, Clarksburg, West Virginia, was named Vice President of the West Virginia State Medical Association at its recent annual meeting held at White Sulphur Springs.

Dr. Charles E. Lyght, Rahway, New Jersey, Director of Medical Publications, Merck Sharp & Dohme Research Laboratories, was recently elected President for 1958 of the American Medical Writers Association.

Dr. Claude S. Beck, Sr., Cleveland, spoke on "Trends in the Surgical Treatment of Coronary Artery Disease" at a professional symposium sponsored by the Gaston County Heart Association, February 3.

Dr. Alton Ochsner, New Orleans, Louisiana, will speak on "Carcinoma of the Lung" at the Chicago Medical Society Clinical Conference at the Palmer House, Chicago, Illinois, March 4-7.

Drs. Leo G. Rigler, Los Angeles California and **Sol Katz,** Washington, D. C., will serve on a panel on diagnostic x-ray functions at the American Academy of General Practice 1958 Scientific Assembly program March 26.

Dr. Eugene T. McEnery, Chicago is the Chairman of the Annual Conference sponsored by the Chicago Medical Society at the Palmer House March 4-7.

Book Reviews

SYMPOSIUM—THE MANAGEMENT OF TUBERCULOSIS, Irving J. Selikoff, Editor. Waverly Press, Baltimore, 1956.

A praiseworthy project of the Journal of the Mount Sinai Hospital materialized when it carried a symposium on the management of tuberculosis in its July-August 1956 issue. Written by members of the Mount Sinai Hospital of New York City and published in book form by the Waverly Press, this work represents an important contribution to current medical literature. It contains a remarkably thorough and competent assaying of modern chemotherapy of this disease, with special attention to problems of pertinent interest, including combination of various antimicrobial agents and occurrence of tubercle bacilli resistant to specific drugs. The data offered are based on extensive clinical material and carry the hallmark of keen observation, and discriminating, prudent judgment. Emphasis on certain therapeutic precepts are derived from personal experience of the authors and augmented by corroborative references. Ample space devoted to the discussion of respiratory function studies, tuberculous pleurisy with effusion, tuberculosis in childhood and pulmonary resection. Other topics which are adequately covered include tuberculous meningitis and lymphadenitis, moreover, genito-urinary, cutaneous and orthopedic forms of tuberculosis. Impressive chapters deal with tuberculoma of the lung, tuberculosis of the larynx and intestines, pregnancy and tuberculosis as well as diabetes and tuberculosis. Discussion of the rehabilitation of the tuberculous patient renders the text a truly comprehensive assay. The book has a pleasing format. It is printed on excellent paper and is enriched with illustrations of technical precision and of highly instructive value.

Andrew L. Banyai, M.D.

EAR, NOSE AND THROAT DYSFUNCTIONS DUE TO DEFICIENCIES AND IMBALANCES. By Dr. Sam E. Roberts. Springfield, Illinois: Charles C Thomas, 1957. Pp. 323, 58 figures. Price: $8.50.

Dr. Morris Fishbein, who contributed the foreword to this book, was impressed by the fact that "Dr. Roberts has wisely recognized that conditions affecting the nose, throat, the sinuses, the nervous system—in fact, any portion of the human body—are in a sense not localized but constitutional disorders. Obviously the attack on a constitutional disorder is not limited to surgical correction of the anatomical errors nor to elimination of infectious or toxic agents. The attack must be total." Dr. Roberts states: "I am certain that deficiencies, and especially imbalances, are the principle causes of the diseases, dysfunctions and syndromes herein reported." In considering such areas of otolaryngological interest as headaches, Meniere's disease, perceptive hearing loss, sore throat, sinus dysfunction and allergy, the author attempts to associate accepted facts concerning metabolic disturbances and nutritional deficiencies with the presenting symptoms of the patients he has observed in almost a half century of practice. By the employment of numerous historic forms the patient indulges in a self analysis of his diet, his habits, his symptoms and other personal historical facts by checking "yes" or "no."

Dr. Roberts has likewise systematized instructions to the allergic patient and specific and general nutritional orders and suggestions on cards prepared for distribution to the patient. Each area of discussion, including those already mentioned, and gonadal, and insulin-sugar imbalances, are supported by case reports to substantiate the author's contention that metabolic disturbances and nutritional deficiencies may affect the ear, nose and throat. He seeks to establish the accepted thesis in this regard by a large number of hypotheses and speculations which he believes to "represent sound basic tenets."

Francis L. Lederer, M.D.

SYMPOSIUM ON TUBERCULOSIS. Edited by F. R. G. Heaf, London, 1957. 755 and xvi pages. 78 plates. 54 figures. 110 tables. 1200 references.

This comprehensive volume by more than a dozen leading British authorities, presents a picture of tuberculosis in England strikingly different from that in the United States today.

Tuberculosis is regarded as a universal infection, its manifestations depending chiefly on differences in resistance of the victims, bovine type infections and extrapulmonary forms accounting for a large part of the morbidity. Diagnosis is chiefly history, physical examination and x-ray, among persons coming in because of symptoms, and treatment is chiefly the collapse therapy, medical and surgical, and chemotherapy with the three drugs, streptomycin, PAS, and INH, with rehabilitation efforts aimed at early return to work, sometimes even while still sputum positive.

In America, where less than 10 per cent of the population under 25 have been infected, 80 per cent of those dying of tuberculosis are over 45 years of age, the importance of frequency and dosage of infection and reinfection is stressed, bovine tuberculosis has been eradicated, and extrapulmonary tuberculosis is only an infrequent occurrence. Diagnosis is sought by routine minifilm screening of hospital admissions, prisoners, pensioners and other large groups with high incidence, and treatment relies chiefly on prolonged chemotherapy, with other agents when the standard triad fails, resection of persistent cavities, and relief from economic pressure by disability and old age pensions and other social security measures.

This contrast is overdrawn, as the authors are themselves aware of the great differences between tuberculosis in England and in the undeveloped countries, in the past and the present, and the rapidly changing picture during the past few years. The differences in epidemiological factors do not obliterate the fundamental identity of the clinical disease, clearly presented in these pages. There is much of value here in the careful conservative marshalling of facts, the objective analysis of the data, the tolerant evaluation of conflicting interpretations, the philosophic acceptance of opposition and the British persistence in the face of obstacles and setbacks.

Emil Bogen, M.D.

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Residents wanted in pulmonary diseases for July 1, 1958. 600-bed hospital in Ozarks. Fully certified, excellent facilities, research and teaching program. Generous salary. Write: Charles A. Brasher, M.D., Superintendent and Medical Director, Missouri State Sanatorium, Mount Vernon, Missouri.

Assistant medical director wanted for 114-bed tuberculosis hospital. Salary $8500-9500 per year, plus complete maintenance including apartment, food, laundry, and utilities. Apply: Executive Director, State Tuberculosis Hospital Commission, New Capitol Annex, Frankfort, Kentucky.

Two physicians wanted for approved residency in tuberculosis and pulmonary diseases. 200-bed hospital, integral part of medical school and of the primary general teaching hospital—residency includes 3 months elective training in related fields such as cardio-pulmonary laboratory, research bacteriology laboratory, infectious diseases. Salary $225 month minimum. Please write to: Medical Director, Woodlawn Hospital, 3819 Maple Avenue, Dallas, Texas.

Full-time staff physician wanted for the Idaho State Tuberculosis Hospital, Gooding, Idaho. New, fully modern hospital building recently completed, replacing several small antiquated units. Total bed capacity of 85. Salary governed by training and experience. Apply: Medical Director, Idaho State Tuberculosis Hospital, Gooding, Idaho.

Wanted: Superintendent and medical director 100-bed tuberculosis sanatorium in Southeastern Minnesota. Completely modern. Well equipped. Ideal consultation and surgical conveniences. Salary open. Address correspondence to Dr. R. F. Sherman, Chairman, Board of Directors, Mineral Springs Sanatorium, Cannon Falls, Minnesota.

Wanted—July 1, 1958, Medical Director and Superintendent for 359-bed modern tuberculosis hospital located in rural scenic area of North Dakota, now averaging 35 patients. 231 admissions in 1957. Patients with non-tuberculous disease admitted for diagnosis. Possibility of transfer of hospital to State University city with faculty appointment for qualified chest physician. U. S. Citizenship, five years experience in tuberculosis and eligibility for state licensure required by state law. Applicant has to acquire medical license at first opportunity following employment. Salary to $14,000 depending upon training, and full family maintenance. Send all particulars, including references, first letter, to Mr. H. H. Joos, Chairman, Board of Administration, Bismarck, North Dakota.

CALENDAR OF EVENTS

National and International Meetings

24th Annual Meeting, American College of Chest Physicians
Fairmont Hotel, San Francisco, June 18-22, 1958

Fifth International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Tokyo, Japan, September 7-11, 1958

Chapter Meetings

APRIL

Alabama Chapter, April 16, Montgomery
Arizona Chapter, April, Chandler
California Chapter, April 26, Los Angeles
Georgia Chapter, April 29, Macon
Illinois Chapter, April 24, Rockford
Louisiana Chapter, April 12, Baton Rouge
Missouri Chapter, April 13, St. Louis
Ohio Chapter, April 16, Cincinnati
Pennsylvania Chapter, April 16, Reading
Tennessee Chapter, April 21, Chattanooga
Texas Chapter, April 20, Houston

MAY

Florida Chapter, May 11, Miami Beach (Bal Harbor)
Mississippi Chapter, May 12, Jackson
Illinois Chapter, May 22, Chicago
New Mexico Chapter, May 16, Albuquerque
Wisconsin Chapter, May 5, Milwaukee

A CORDIAL WELCOME AWAITS YOU IN TOKYO

Fifth International Congress

on

Diseases of the Chest

September 7-11, 1958

Inaugural Ceremony
September 7—Homiuri Hall

Congress Banquet
September 10—Tokyo Kaikan

Scientific Program

Formal presentations
Panel discussions
Fireside conferences
Motion pictures

Scientific exhibits
Technical Exhibits
Visits to hospitals and universities

Social Program

Receptions
Tea ceremonies
Japanese musical

Japanese dining—tours and sightseeing

Program Topics

Radiation Hazards
Coronary Disease
Occupational Diseases
Effects of Jet Air Travel
Chest Tumors
Tuberculosis
Asthma and Emphysema
Cardiopulmonary Physiology
Bronchoesophagology
Cardiovascular Surgery
Tropical Diseases
Lung Cancer
Pediatric Cardiology
and
Miscellaneous subjects
on
Diseases of the Chest

For further information and for the name of the official travel agent in your area—please write

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American College of Chest Physicians
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Important!

San Francisco Hotel Reservations

24th ANNUAL MEETING, AMERICAN COLLEGE OF CHEST PHYSICIANS

Fairmont Hotel, San Francisco, June 18-22, 1958

Members planning to attend *only* the College meeting in San Francisco must complete the coupon on this page and mail it to the Convention Bureau together with a deposit in the amount of $10.00 for each room requested.

Members planning to attend the College meeting and *all or a portion* of the meeting of the American Medical Association, June 23-27, must attach a room reservation form clipped from an issue of the Journal of the A.M.A. to the form appearing below and mail *both coupons*, together with a deposit in the amount of $10.00 per room, directly to the San Francisco Convention and Visitors Bureau.

Members of the College are urged to submit their reservation forms to the San Francisco Convention and Visitors Bureau at the earliest possible date in order to be assured of satisfactory accommodations.

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San Francisco Convention and Visitors Bureau
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I am planning to attend the 24th ANNUAL MEETING, AMERICAN COLLEGE OF CHEST PHYSICIANS, FAIRMONT HOTEL, SAN FRANCISCO, JUNE 18-22, 1958. Please reserve the following accommodations for which I am enclosing a deposit in the amount of $10.00.

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